10/798,3176

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:sssptasel1626

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	SEP 01	New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover!
NEWS	4	OCT 28	KOREAPAT now available on STN
NEWS	5	NOV 30	PHAR reloaded with additional data
NEWS	6	DEC 01	LISA now available on STN
NEWS	7	DEC 09	12 databases to be removed from STN on December 31, 2004
NEWS	8	DEC 15	MEDLINE update schedule for December 2004
NEWS	9	DEC 17	ELCOM reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	10	DEC 17	COMPUAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	11	DEC 17	SOLIDSTATE reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	12	DEC 17	CERAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	13	DEC 17	THREE NEW FIELDS ADDED TO IFIPAT/IFIUDB/IFICDB
NEWS	14	DEC 30	EPFULL: New patent full text database to be available on STN
NEWS	15	DEC 30	CAPLUS - PATENT COVERAGE EXPANDED
NEWS	16	JAN 03	No connect-hour charges in EPFULL during January and February 2005
NEWS	17	FEB 25	CA/CAPLUS - Russian Agency for Patents and Trademarks (ROSPATENT) added to list of core patent offices covered
NEWS	18	FEB 10	STN Patent Forums to be held in March 2005
NEWS	19	FEB 16	STN User Update to be held in conjunction with the 229th ACS National Meeting on March 13, 2005
NEWS	20	FEB 28	PATDPAFULL - New display fields provide for legal status data from INPADOC
NEWS	21	FEB 28	BABS - Current-awareness alerts (SDIs) available
NEWS	22	FEB 28	MEDLINE/LMEDLINE reloaded
NEWS	23	MAR 02	GBFULL: New full-text patent database on STN
NEWS	24	MAR 03	REGISTRY/ZREGISTRY - Sequence annotations enhanced
NEWS	25	MAR 03	MEDLINE file segment of TOXCENTER reloaded

NEWS EXPRESS	JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 13:13:05 ON 04 MAR 2005

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 13:13:16 ON 04 MAR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 2 MAR 2005 HIGHEST RN 841200-41-7
DICTIONARY FILE UPDATES: 2 MAR 2005 HIGHEST RN 841200-41-7

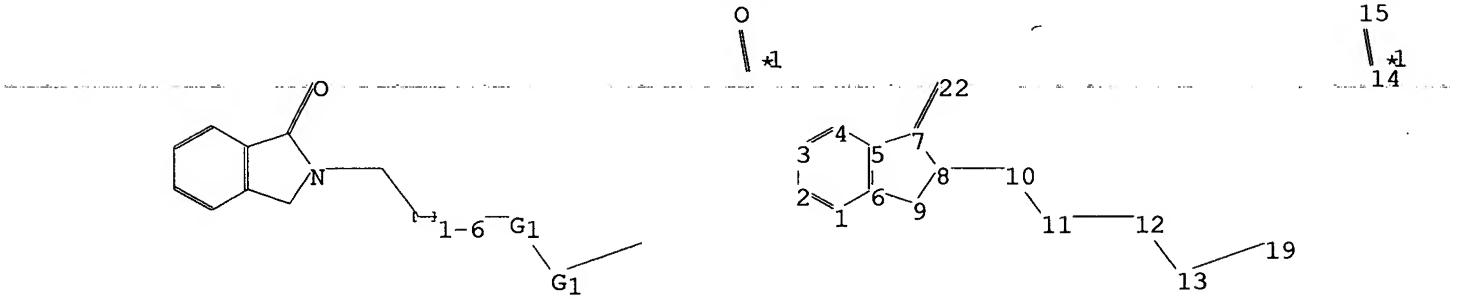
TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\Program Files\Stnexp\Queries\10798372.str



chain nodes :
10 11 12 13 14 15 19 22
ring nodes :
1 2 3 4 5 6 7 8 9
chain bonds :
7-22 8-10 10-11 11-12 12-13 13-19 14-15
ring bonds :

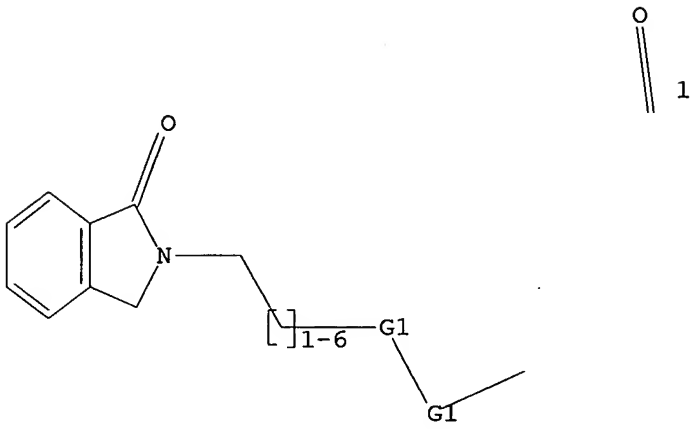
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9
exact/norm bonds :
5-7 6-9 7-8 7-22 8-9 8-10 11-12 12-13 13-19 14-15
exact bonds :
10-11
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

G1:N,[*1]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 19:CLASS 22:CLASS

L1 STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1 STR



G1 N,[@1]

Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 13:13:33 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 6380 TO ITERATE

15.7% PROCESSED 1000 ITERATIONS 11 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 122812 TO 132388
PROJECTED ANSWERS: 901 TO 1905

L2 11 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 13:13:40 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 128438 TO ITERATE

100.0% PROCESSED 128438 ITERATIONS 2400 ANSWERS
SEARCH TIME: 00.00.01

L3 2400 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 161.33 161.54

FILE 'CAPLUS' ENTERED AT 13:13:44 ON 04 MAR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 4 Mar 2005 VOL 142 ISS 11
FILE LAST UPDATED: 3 Mar 2005 (20050303/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 637 L3

=> file reg
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 0.45 161.99

FILE 'REGISTRY' ENTERED AT 13:14:17 ON 04 MAR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 2 MAR 2005 HIGHEST RN 841200-41-7
DICTIONARY FILE UPDATES: 2 MAR 2005 HIGHEST RN 841200-41-7

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

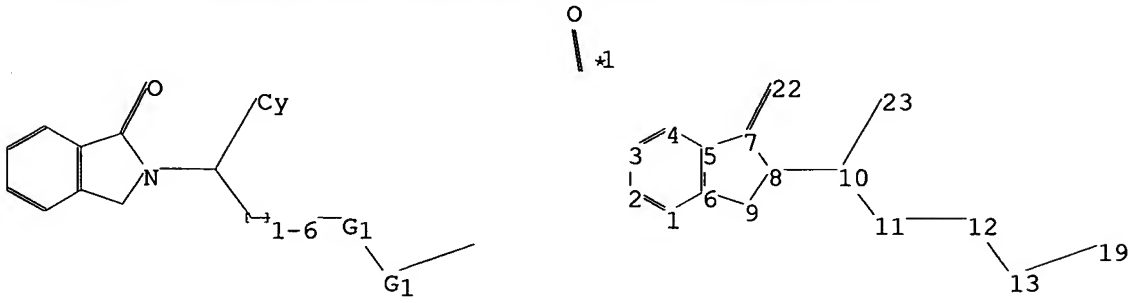
Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:

http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\Program Files\Stnexp\Queries\10798372b.str



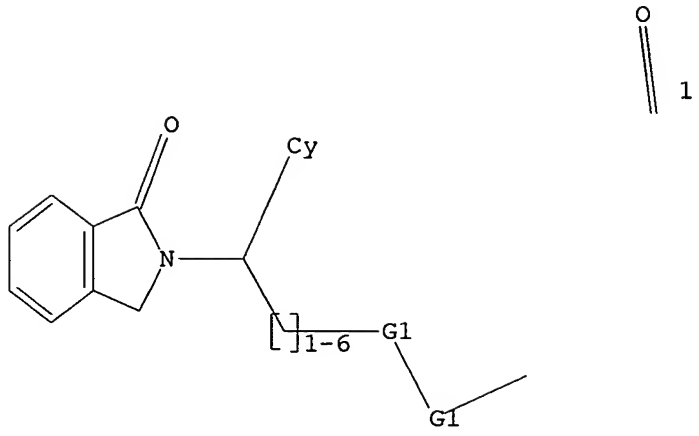
chain nodes :
10 11 12 13 14 15 19 22 23
ring nodes :
1 2 3 4 5 6 7 8 9
chain bonds :
7-22 8-10 10-11 10-23 11-12 12-13 13-19 14-15
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9
exact/norm bonds :
5-7 6-9 7-8 7-22 8-9 8-10 10-23 11-12 12-13 13-19 14-15
exact bonds :
10-11
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

G1:N,[*1]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 19:CLASS 22:CLASS 23:Atom

L5 STRUCTURE UPLOADED

=> d
L5 HAS NO ANSWERS
L5 STR



G1 N,[@1]

Structure attributes must be viewed using STN Express query preparation.

=> s l5
SAMPLE SEARCH INITIATED 13:14:35 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 6380 TO ITERATE

15.7% PROCESSED 1000 ITERATIONS 0 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 122812 TO 132388
PROJECTED ANSWERS: 0 TO 0

L6 0 SEA SSS SAM L5

=> s l5 full
FULL SEARCH INITIATED 13:14:38 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 128430 TO ITERATE

100.0% PROCESSED 128430 ITERATIONS 66 ANSWERS
SEARCH TIME: 00.00.02

L7 66 SEA SSS FUL L5

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	161.33	323.32

FILE 'CAPLUS' ENTERED AT 13:14:44 ON 04 MAR 2005

FILE COVERS 1907 - 4 Mar 2005 VOL 142 ISS 11
FILE LAST UPDATED: 3 Mar 2005 (20050303/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l7
L8 22 L7

=> d ibib abs hitstr tot
THE ESTIMATED COST FOR THIS REQUEST IS 108.68 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:y

instant app

L8 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:780510 CAPLUS
DOCUMENT NUMBER: 141:277486
TITLE: A preparation of 7-aminoisoindolone derivatives
INVENTOR(S): Man, Hon-Wah; Muller, George W.; Zhang, Weihong
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004080423	A2	20040923	WO 2004-US7743	20040312
WO 2004080423	A3	20041104		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004254214	A1	20041216	US 2004-798317	20040312
PRIORITY APPLN. INFO.:			US 2003-454155P	P 20030312
OTHER SOURCE(S):	MARPAT 141:277486			

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

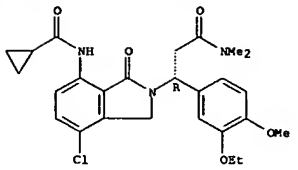
AB The invention relates to a preparation of 7-aminoisoindole derivs. of formula I [wherein: Y is C(O), CH2, CH2C(O), or SO2; X is H; Z is -alkyl-CO2H, alkyl, -alkyl-OH, or -alkyl-NH2, etc.; R1 and R2 are independently selected from (cyclo)alkyl or -alkyl-cycloalkyl], useful for treatment, prevention or management of cancer, inflammatory bowel disease, and myelodysplastic syndrome, etc. (no biol. data). For instance, isoindole derivative II was prepared via heterocyclization of aminopropanol derivative III and benzoic acid derivative IV with a yield of 64% (example 1).

IT 760958-97-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminoisoindolone derivs. via heterocyclization of aminopropanol derivs. and benzoic acid derivs.)

RN 760958-97-2 CAPLUS
CN 2H-Isoindole-2-propanamide, 4-chloro-7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L8 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:780509 CAPLUS
DOCUMENT NUMBER: 141:295861
TITLE: A preparation of novel isoindolone derivatives, useful as PDE4 inhibitors
INVENTOR(S): Man, Hon-Wah; Muller, George W.
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004080422	A2	20040923	WO 2004-US7742	20040312
WO 2004080422	A3	20041028		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004259873	A1	20041223	US 2004-798372	20040312
PRIORITY APPLN. INFO.:			US 2003-454149P	P 20030312
OTHER SOURCE(S):	MARPAT 141:295861			

GI

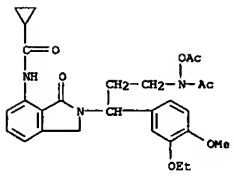
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a preparation of novel isoindolone derivs. of formula I [wherein: Y is C(O), CH2, CH2C(O), or SO2; R1 and R2 are independently selected from (cyclo)alkyl, CF2H, CF3, or CH2CHF2, etc.; Z1 is H, alkyl, NH2, or NH2, etc.; Z2 is H or CHO, -C(O)-alkyl, or -C(O)Ph, etc.; X1, X2, X3, and X4 are independently selected from H, halogen, NO2, CF3, alkyl, or alkylimidazolyl, etc.; R3 and R4 are independently H or alkyl], useful for treatment or prevention of various diseases and disorders, for example, diseases associated with PDE4 (no biol. data). For instance, isoindolone derivative II was prepared via amination of N-(hydroxypropyl)isoindolone derivative III by N,O-(tert-butoxycarbonyl)hydroxylamine with a yield of 78% (example 3).

IT 761434-30-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of novel isoindolone derivs., useful as PDE4 inhibitors)

RN 761434-30-4 CAPLUS
CN Cyclopropanecarboxamide, N-[2-[3-[acetyl(acetyloxy)amino]-1-(3-ethoxy-4-methoxyphenyl)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

L8 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

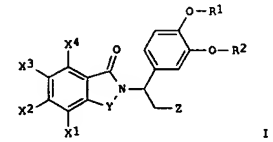


L8 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN

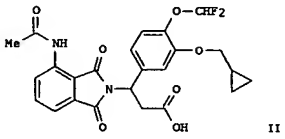
ACCESSION NUMBER: 2004:589381 CAPLUS
DOCUMENT NUMBER: 141:140314
TITLE: Preparation of 2-(fluoroalkoxyphenylalkyl)-1,3-dihydroisoindolones as PDE4, TNF-α, and/or MMP inhibitors
INVENTOR(S): Muller, George W.; Man, Hon-Wah; Zhang, Weihong
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004060313	A2	20040722	WO 2003-US41568	20031229
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004204448	A1	20041014	US 2003-748085	20031229
PRIORITY APPLN. INFO.:			US 2002-436975P	P 20021230
OTHER SOURCE(S):		MARPAT 141:140314		

GI



I



II

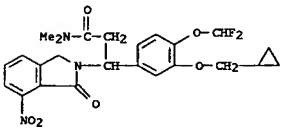
AB Title compds. I [wherein X1-X4 = independently H, halo, NO2, NH2, CF3,

L8 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

alkyl, cycloalkyl(alkyl), NR7R8-(alkyl), R8CONH-(alkyl), NR7R8CONH-(alkyl), R8OCONH-(alkyl), R8O-(alkyl), imidazolyl(alkyl), pyrrolyl(alkyl), oxadiazolyl(alkyl), triazolyl(alkyl); or X1 and X2 or X2 and X3 or X3 and X4 may be taken together to form a (hetero)cycloalkyl ring; Y = CO, CH2, CH2CO, COCH2, SO2; Z = H, COR3, alkylsulfonyl(alkyl), alkyl, CH2OH, alkoxymethyl, CN; R1 and R2 = independently CHF2, alkyl, cycloalkyl(alkyl); at least one of R1 and R2 = CHF2; R3 = NR4R5, alkyl, OH, alkoxy, (un)substituted Ph, PhCH2; R4 and R5 = independently H, alkyl, OH, OCOR6; R6 = alkyl(amino), Ph, PhCH2, aryl; R7 and R8 = independently H, alkyl, cycloalkyl(alkyl), NR7R8-alkyl, R8O-alkyl, Ph, PhCH2, aryl; or pharmaceutically acceptable salts, hydrates, solvates, clathrates, stereoisomers, and prodrugs thereof] were prepd. For example, alkylation of 3,4-dihydroxybenzaldehyde with chlorodifluoromethane in the presence of K2CO3 in DMF gave 4-difluoromethoxy-3-hydroxybenzaldehyde (15%), which was further alkylated with bromomethylcyclopropane under the same conditions to afford 3-cyclopropylmethoxy-4-difluoromethoxybenzaldehyde (100%). Reaction of the benzaldehyde with ammonium acetate in 95% EtOH, followed by addn. of malonic acid provided 3-amino-3-(3-cyclopropylmethoxy-4-difluoromethoxyphenyl)propionic acid (52%). Condensation of the amine with 3-acetamidophthalic anhydride using sodium acetate in AcOH yielded the isoindoledione II (85%). I and their pharmaceutical compns., optionally in combination with another therapeutic agent, are useful for the treatment or prevention of diseases assocd. with phosphodiesterase 4 (PDE4) inhibition, abnormal tumor necrosis factor α (TNF-α) levels , and/or matrix metalloproteinase (MMP) inhibition, such as myelodysplastic syndrome, myeloproliferative disease, complex regional pain syndrome, cancer, inflammatory diseases, and autoimmune diseases (no data).

IT **725256-78-0P**, 3-[3-(Cyclopropylmethoxy)-4-difluoromethoxyphenyl]-3-(7-nitro-1-oxo-1,3-dihydroisoindol-2-yl)-N,N-dimethylpropionamide
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(PDE4, TNF-α, and/or MMP inhibitor; preparation of (fluoroalkoxyphenylalkyl)isoindolones as PDE4, TNF-α, and/or MMP inhibitors for treatment of inflammatory diseases, autoimmune diseases, cancer, and pain)

RN 725256-78-0 CAPLUS
CN 2H-Isoindole-2-propanamide, β-[3-(cyclopropylmethoxy)-4-(difluoromethoxy)phenyl]-1,3-dihydro-N,N-dimethyl-7-nitro-1-oxo- (9CI) (CA INDEX NAME)

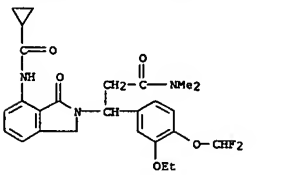


IT **725256-71-3P**, 3-(4-Acetylamino-1,3-dioxo-1,3-dihydroisoindol-2-yl)-3-[3-(cyclopropylmethoxy)-4-difluoromethoxyphenyl]-N,N-dimethylpropionamide **725256-79-1P**, 3-(7-Amino-1-oxo-1,3-dihydroisoindol-2-yl)-3-[3-(cyclopropylmethoxy)-4-difluoromethoxyphenyl]-N,N-dimethylpropionamide **725256-89-3P**, Cyclopropanecarboxylic acid N-[2-[1-(4-difluoromethoxy-3-ethoxyphenyl)-2-

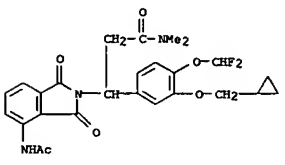
L8 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

(dimethylcarbamoyl)ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl]amide **725256-92-8P**, 3-(7-Acetylamino-1-oxo-1,3-dihydroisoindol-2-yl)-3-(4-difluoromethoxy-3-ethoxyphenyl)-N,N-dimethylpropionamide **725256-96-2P**, 3-(4-Acetylamino-1,3-dioxo-1,3-dihydroisoindol-2-yl)-3-(4-difluoromethoxy-3-ethoxyphenyl)-N,N-dimethylpropionamide **725257-06-7P**, 3-(4-Acetylamino-1,3-dioxo-1,3-dihydroisoindol-2-yl)-3-[3,4-bis(difluoromethoxy)phenyl]-N,N-dimethylpropionamide **725257-11-4P**, Cyclopropanecarboxylic acid N-[2-[1-[3,4-bis(difluoromethoxy)phenyl]-2-(dimethylcarbamoyl)ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl]amide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(PDE4, TNF-α, and/or MMP inhibitor; prepn. of (fluoroalkoxyphenylalkyl)isoindolones as PDE4, TNF-α, and/or MMP inhibitors for treatment of inflammatory diseases, autoimmune diseases, cancer, and pain)

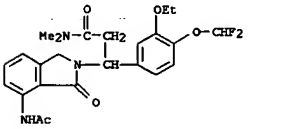
RN 725256-71-3 CAPLUS
CN 2H-Isoindole-2-propanamide, 4-(acetylamino)-β-[3-(cyclopropylmethoxy)-4-(difluoromethoxy)phenyl]-1,3-dihydro-N,N-dimethyl-1,3-dioxo- (9CI) (CA INDEX NAME)



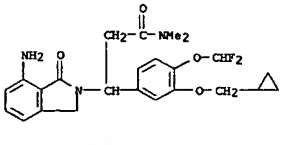
RN 725256-92-8 CAPLUS
CN 2H-Isoindole-2-propanamide, 7-(acetylamino)-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-N,N-dimethyl-1-oxo- (9CI) (CA INDEX NAME)



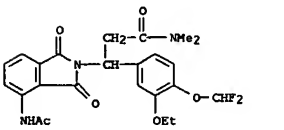
RN 725256-79-1 CAPLUS
CN 2H-Isoindole-2-propanamide, 7-amino-β-[3-(cyclopropylmethoxy)-4-(difluoromethoxy)phenyl]-1,3-dihydro-N,N-dimethyl-1-oxo- (9CI) (CA INDEX NAME)



RN 725256-96-2 CAPLUS
CN 2H-Isoindole-2-propanamide, 4-(acetylamino)-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-N,N-dimethyl-1,3-dioxo- (9CI) (CA INDEX NAME)

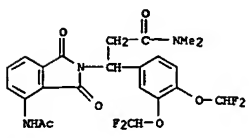


RN 725256-89-3 CAPLUS
CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-N,N-dimethyl-1-oxo- (9CI) (CA INDEX NAME)

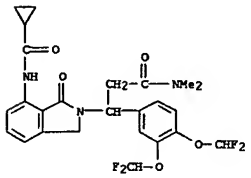


RN 725257-06-7 CAPLUS
CN 2H-Isoindole-2-propanamide, 4-(acetylamino)-β-[3,4-bis(difluoromethoxy)phenyl]-1,3-dihydro-N,N-dimethyl-1,3-dioxo- (9CI) (CA INDEX NAME)

L8 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 725257-11-4 CAPLUS
CN 2H-Isoindole-2-propanamide, β-[3,4-bis(difluoromethoxy)phenyl]-7-[(cyclopropylcarbonyl)amino]-1,3-dihydro-N,N-dimethyl-1-oxo- (9CI) (CA INDEX NAME)

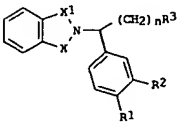


L8 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:1001604 CAPLUS
DOCUMENT NUMBER: 140:42030
TITLE: Preparation of isoindolinediones as angiogenesis inhibitors.
INVENTOR(S): Man, Hon-wah; Muller, George W.
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: U.S., 28 pp., Cont.-in-part of U.S. Ser. No. 590,344.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6667316	B1	20031223	US 2000-708199	20001108
CA 2392081	AA	20010517	CA 2000-2392081	20001109
WO 2001034606	A1	20010517	WO 2000-US30770	20001109
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1228071	A1	20020807	EP 2000-977095	20001109
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NZ 519459	A	20031128	NZ 2000-519459	20001109
JP 2004500346	T2	20040108	JP 2001-536553	20001109
NO 2002002223	A	20020708	NO 2002-2223	20020508
FI 2002000892	A	20020510	FI 2002-892	20020510
US 2004147588	A1	20040729	US 2003-685942	20031014

PRIORITY APPLN. INFO.:
US 1999-165168P P 19991112
US 2000-590344 A2 20000608
US 2000-708199 A 20001108
WO 2000-US30770 W 20001109

OTHER SOURCE(S): MARPAT 140:42030
GI



I

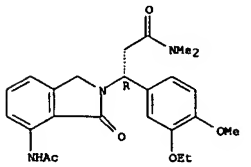
AB Title compds. [I; R1, R2 = alkyl, alkoxy, cyano, cycloalkoxy, cycloalkyl, cycloalkylmethoxy; 1 of X and X1 = CO, SO2 and the other of X and X1 = CO, CH2, SO2, CH2CO; R3 = SO2Y, CO2, CN, hydroxyalkyl; Y = alkyl, Ph, PhCH2; Z = NR61R71, alkyl, Ph, PhCH2; R61 = H, alkyl, cycloalkyl, Ph, PhCH2, etc.; R71 = alkyl; 1 of R4, R5 = H and the other = imidazolyl, pyrrolyl,

L8 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
oxadiazolyl, triazolyl, R6R7N(CzH2z); z = 0, 1; n = 1-3; R6 = cycloalkanoyl which is unsubstituted or substituted with halo, amino, monoalkylamino, dialkylamino; R4R5 = NHCH2R8, NHCOR8, N:CHR8; R7 = H, alkyl, methylsulfonyl, alkoxyalkylcarbonyl; R8 = CH2, O, NH, CH:CH, CH:N], were prepd. for treatment of undesirable angiogenesis (no data). Thus, 3,4-dinitrophthalic acid and 2-(3-ethoxy-4-methoxyphenyl)-1-(methylsulfonyl)eth-2-ylamine in PhMe were refluxed for 15 h through a Dean-Stark trap to give 49% 2-[1-(3-Ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4,5-dinitroisoindoline-1,3-dione. This was hydrogenated in EtOAc over Pd/C to give 73% 2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4,5-diaminoisoindoline-1,3-dione. The latter was refluxed 17 h with DMF di-Me acetal in HOAc to give 68% 7-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-3-pyrrolino[3,4-e]benzimidazole-6,8-dione.

IT **340019-71-8P 340019-72-9P 340019-73-0P 340019-75-2P 340019-76-3P 635705-68-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of isoindolinediones as angiogenesis inhibitors)

RN 340019-71-8 CAPLUS
CN 2H-Isoindole-2-propanamide, 7-(acetylamino)-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

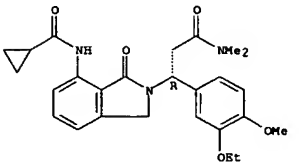
Absolute stereochemistry.



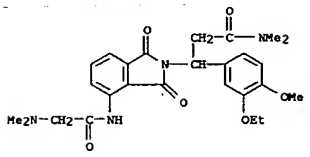
RN 340019-72-9 CAPLUS
CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



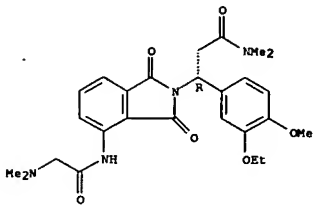
RN 340019-73-0 CAPLUS
CN 2H-Isoindole-2-propanamide, 4-[[(dimethylamino)acetyl]amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1,3-dioxo-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

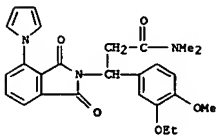
RN 340019-75-2 CAPLUS
CN 2H-Isoindole-2-propanamide, 4-[[(dimethylamino)acetyl]amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1,3-dioxo-, monohydrochloride, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



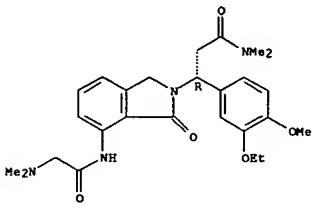
● HCl

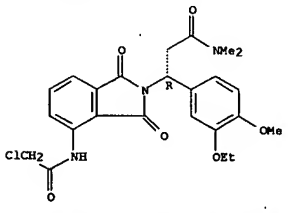
RN 340019-76-3 CAPLUS
CN 2H-Isoindole-2-propanamide, β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1,3-dioxo-4-(1H-pyrrol-1-yl)- (9CI) (CA INDEX NAME)



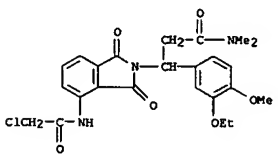
RN 635705-68-9 CAPLUS
CN 2H-Isoindole-2-propanamide, 7-[[(dimethylamino)acetyl]amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

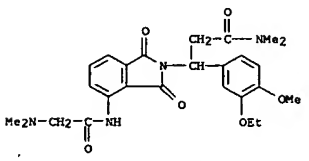




IT **340019-93-4P 340019-94-5P 340019-95-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of isoindolinediones as angiogenesis inhibitors)
RN 340019-93-4 CAPLUS
CN 2H-Isoindole-2-propanamide, 4-[(chloroacetyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1,3-dioxo- (9CI) (CA INDEX NAME)



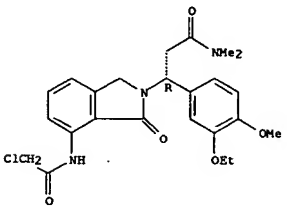
RN 340019-94-5 CAPLUS
CN 2H-Isoindole-2-propanamide, 4-[[(dimethylamino)acetyl]amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1,3-dioxo- (9CI) (CA INDEX NAME)



RN 340019-95-6 CAPLUS
CN 2H-Isoindole-2-propanamide, 4-[[(dimethylamino)acetyl]amino]-β-(3-

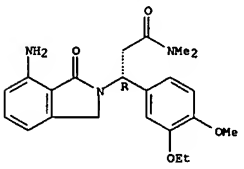
IT **340019-74-1 340020-04-4 635705-78-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of isoindolinediones as angiogenesis inhibitors)
RN 340019-74-1 CAPLUS
CN 2H-Isoindole-2-propanamide, 7-[(chloroacetyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 340020-04-4 CAPLUS
CN 2H-Isoindole-2-propanamide, 7-amino-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

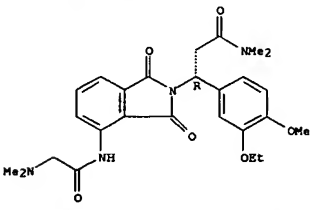


RN 635705-78-1 CAPLUS
CN 2H-Isoindole-2-propanamide, 4-[(chloroacetyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1,3-dioxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1,3-dioxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN

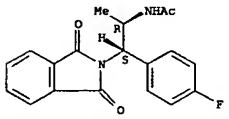
ACCESSION NUMBER: 2002:603331 CAPLUS
DOCUMENT NUMBER: 138:247919
TITLE: Synthesis and antitumor activity of enantiomerically pure [1,2-diamino-1-(4-fluorophenyl)propane]dichloroplatinum(II) complexes
AUTHOR(S): Dufrasne, Francois; Gelbcke, Michael; Schnurr, Beate; Gust, Ronald
CORPORATE SOURCE: Laboratoire de Chimie Pharmaceutique Organique, Institut de Pharmacie, Universite Libre de Bruxelles, Brussels, Belg.
SOURCE: Archiv der Pharmazie (Weinheim, Germany) (2002), 335(5), 229-239
CODEN: ARPMAS; ISSN: 0365-6233
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:247919

AB Enantiomerically pure 1,2-diamino-1-(4-fluorophenyl)propanes were synthesized by stereospecific and stereoselective procedures by use of the (1R,2S)- and (1S,2R)-2-amino-1-(4-fluorophenyl)propanols as intermediates. The enantiomeric purity was determined by 1H NMR spectroscopy after conversion of the propanolamines and the diamines with (1R)-myrtenal into mono- and diimines. For the coordination to platinum the diamines were reacted with K2PtCl4. The resulting dichloroplatinum(II) complexes 4F-Ph/Me-PtCl2 were tested for antiproliferative activity on the MCF-7 breast cancer cell line. (SS)- and (RR)-4F-Ph/Me-PtCl2 produced the strongest inhibitory effect. Both complexes showed cytocidal effects, (SS)-4F-Ph/Me-PtCl2 even in a concentration of 1 μM. The (1S,2R)- and (1R,2S)- configurated complexes were far less active (SS > RR > RS = SR) and comparable in this respect with the standard cisplatin.

IT 502850-18-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and antitumor activity of enantiomerically pure [diamino(fluorophenyl)propane]dichloroplatinum(II) complexes)

RN 502850-18-2 CAPLUS
CN Acetamide, N-[(1R,2S)-2-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)-2-(4-fluorophenyl)-1-methylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN

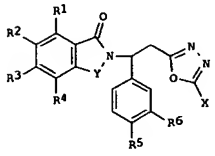
ACCESSION NUMBER: 2001:472708 CAPLUS
DOCUMENT NUMBER: 135:76876
TITLE: Preparation of 2-(1,3,4-oxadiazol-2-yl)ethylisoindoline-1,3-diones as phosphodiesterase 4 inhibitors which decrease tumor necrosis factor-α levels
INVENTOR(S): Man, Hon-Wah; Muller, George
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001046183	A1	20010628	WO 2000-US34457	20001219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6326388	B1	20011204	US 1999-470203	19991221
CA 2394615	AA	20010628	CA 2000-2394615	20001219
EP 1242413	A1	20020925	EP 2000-986568	20001219
EP 1242413	B1	20041117		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003518115	T2	20030603	JP 2001-547093	20001219
EP 1462449	A1	20040929	EP 2004-3830	20001219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
AT 282612	E	20041215	AT 2000-986568	20001219
EP 1510518	A2	20050302	EP 2004-20108	20001219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NO 2002002937	A	20020815	NO 2002-2937	20020618
FI 2002001192	A	20020619	FI 2002-1192	20020619

PRIORITY APPLN. INFO.: US 1999-470203 A 19991221
EP 2000-986568 A3 20001219
WO 2000-US34457 W 20001219

OTHER SOURCE(S): MARPAT 135:76876
GI

L8 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

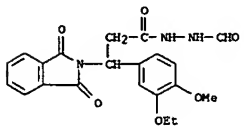


I

AB Title compds. (I; Y = CO, CH2, SO2, CH2CO; X = H, alkyl; R1-R4 = H, halo, CF3, Ac, alkyl, alkoxy, NO2, cyano, OH, CMe3, etc.; adjacent R1-R4 = atoms to form with the Ph ring a naphthylidene, quinoline, quinoxaline, benzimidazole, benzodioxole, or 2-hydroxybenzimidazole ring; R5, R6 = H, alkyl, alkoxy, cyano, benzocycloalkoxy, cycloalkoxy, etc.), were prepared for treatment of inflammation, autoimmune disease, and cancer (no data). Thus, 3-(3-cyclopentyloxy-4-methoxyphenyl)-3-(5-methyl-1,3-dioxoisoindolin-2-yl)propanoic acid, carbonyldiimidazole, and formic hydrazide were stirred in EtOAc to give crude N-carbonylamino-3-(3-cyclopentyloxy-4-methoxyphenyl)-3-(5-methyl-1,3-dioxoisoindolin-2-yl)propanamide, which was treated with POCl3 in MeCN to give 32% 2-[1-(3-cyclopentyloxy-4-methoxyphenyl)-2-(1,3,4-oxadiazol-2-yl)ethyl]-5-methylisoindoline-1,3-dione. Drug formulations containing the latter are given.

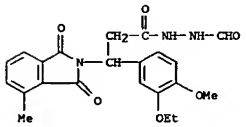
IT 347192-01-2P 347192-05-6P 347192-06-7P
347192-07-8P 347192-08-9P 347192-09-0P
347192-10-3P 347192-11-4P 347192-12-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of oxadiazolylethylisoindolinediones as phosphodiesterase 4 inhibitors which decrease tumor necrosis factor-α levels)

RN 347192-01-2 CAPLUS
CN 2H-Isoindole-2-propanoic acid, β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1,3-dioxo-, 2-formylhydrazide (9CI) (CA INDEX NAME)

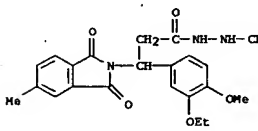


RN 347192-05-6 CAPLUS
CN 2H-Isoindole-2-propanoic acid, β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-4-methyl-1,3-dioxo-, 2-formylhydrazide (9CI) (CA INDEX NAME)

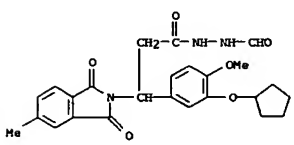
L8 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 347192-06-7 CAPLUS
CN 2H-Isoindole-2-propanoic acid, β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-5-methyl-1,3-dioxo-, 2-formylhydrazide (9CI) (CA INDEX NAME)

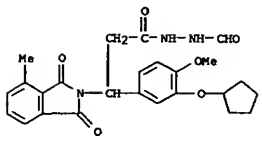


RN 347192-07-8 CAPLUS
CN 2H-Isoindole-2-propanoic acid, β-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,3-dihydro-5-methyl-1,3-dioxo-, 2-formylhydrazide (9CI) (CA INDEX NAME)

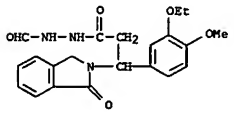


RN 347192-08-9 CAPLUS
CN 2H-Isoindole-2-propanoic acid, β-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,3-dihydro-4-methyl-1,3-dioxo-, 2-formylhydrazide (9CI) (CA INDEX NAME)

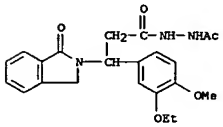
L8 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



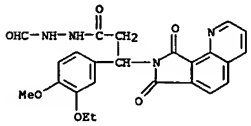
RN 347192-09-0 CAPLUS
CN 2H-Isoindole-2-propanoic acid, β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, 2-formylhydrazide (9CI) (CA INDEX NAME)



RN 347192-10-3 CAPLUS
CN 2H-Isoindole-2-propanoic acid, β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, 2-acetylhydrazide (9CI) (CA INDEX NAME)

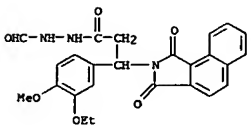


RN 347192-11-4 CAPLUS
CN 8H-Pyrrolo[3,4-h]quinoline-8-propanoic acid, β-(3-ethoxy-4-methoxyphenyl)-7,9-dihydro-7,9-dioxo-, 2-formylhydrazide (9CI) (CA INDEX NAME)



L8 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

RN 347192-12-5 CAPLUS
CN 2H-Benz[e]isoindole-2-propanoic acid, β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1,3-dioxo-, 2-formylhydrazide (9CI) (CA INDEX NAME)



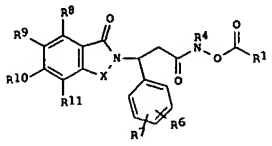
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:472490 CAPLUS
DOCUMENT NUMBER: 135:76791
TITLE: Preparation of 1,3-dioxoisoindolin-2-yl-N-acyloxypropanamides as phosphodiesterase 4 inhibitors which reduce undesirable levels of tumor necrosis factor-α.
INVENTOR(S): Man, Hon-Wah; Muller, George; Huang, Shaei Y.
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001045702	A1	20010628	WO 2000-US34455	20001219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6699899	B1	20040302	US 1999-468529	19991221
CA 2394604	AA	20010628	CA 2000-2394604	20001219
EP 1246620	A1	20021009	EP 2000-988151	20001219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003518060	T2	20030603	JP 2001-546641	20001219
NZ 519638	A	20030926	NZ 2000-519638	20001219
NO 2002002936	A	20020814	NO 2002-2936	20020618
FI 2002001193	A	20020731	FI 2002-1193	20020619
US 2004167174	A1	20040826	US 2004-786822	20040225
PRIORITY APPLN. INFO.:			US 1999-468529 A	19991221
			WO 2000-US34455 W	20001219

OTHER SOURCE(S): MARPAT 135:76791
GI



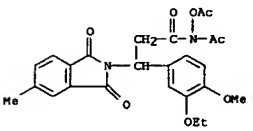
I

AB Title compds. (I; R4 = H, COR12; R1, R12 = alkyl, Ph, PhCH2, pyridyl, pyridylmethyl, imidazolyl, imidazolylmethyl, etc.; X = CO, CH2, CH2CO, SO2; R6, R7 = NO2, cyano, CF3, EtO2C, Ac, AcO, CO2H, OH, amino, etc.; R8-R11 = H, NO2, cyano, CF3, EtO2C, MeO2C, Ac, carbamoyl, AcO, CO2H, amino, acylamino, etc.; or R8R9, R10R11 = benzo, quinolino, quinoxalino, etc.; R9R10 = benzo), were prepd. as drugs (no data). Thus, 3-(1,3-dioxoisoindolin-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propanehydroxamic acid was stirred with propionic anhydride in MeCN overnight to give [3-(1,3-dioxoisoindolin-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propanoylamino]propanoate. Drug formulations contg. the latter were given.

IT **347144-41-6P 347144-42-7P 347144-43-8P**
347144-44-9P 347144-45-0P 347144-46-1P
347144-59-6P 347144-60-9P 347144-61-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1,3-dioxoisoindolin-2-yl-N-acyloxypropanamides as phosphodiesterase 4 inhibitors which reduce undesirable levels of tumor necrosis factor-α)

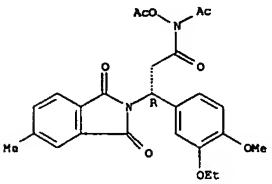
L8 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

RN 347144-41-6 CAPLUS
CN 2H-Isoindole-2-propanamide, N-acetyl-N-(acetyloxy)-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-5-methyl-1,3-dioxo- (9CI) (CA INDEX NAME)



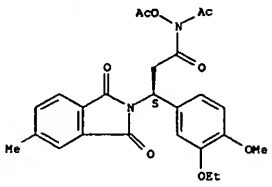
RN 347144-42-7 CAPLUS
CN 2H-Isoindole-2-propanamide, N-acetyl-N-(acetyloxy)-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-5-methyl-1,3-dioxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

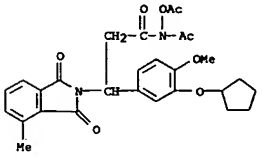


RN 347144-43-8 CAPLUS
CN 2H-Isoindole-2-propanamide, N-acetyl-N-(acetyloxy)-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-5-methyl-1,3-dioxo-, (βS)- (9CI) (CA INDEX NAME)

L8 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
Absolute stereochemistry.

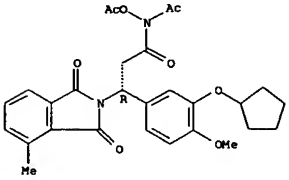


RN 347144-44-9 CAPLUS
CN 2H-Isoindole-2-propanamide, N-acetyl-N-(acetyloxy)-β-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,3-dihydro-4-methyl-1,3-dioxo- (9CI) (CA INDEX NAME)



RN 347144-45-0 CAPLUS
CN 2H-Isoindole-2-propanamide, N-acetyl-N-(acetyloxy)-β-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,3-dihydro-4-methyl-1,3-dioxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

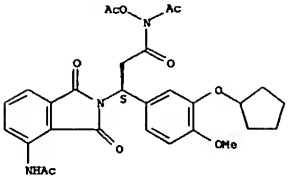


RN 347144-46-1 CAPLUS
CN 2H-Isoindole-2-propanamide, N-acetyl-N-(acetyloxy)-β-[3-

L8 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

RN 347144-61-0 CAPLUS
CN 2H-Isoindole-2-propanamide, N-acetyl-4-(acetylamino)-N-(acetyloxy)-β-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,3-dihydro-1,3-dioxo-, (βS)- (9CI) (CA INDEX NAME)

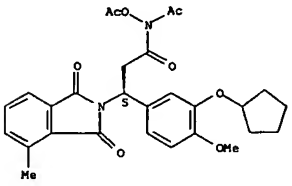
Absolute stereochemistry.



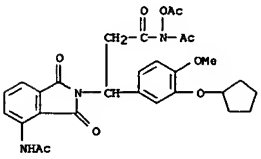
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
(Cyclopentyloxy)-4-methoxyphenyl]-1,3-dihydro-4-methyl-1,3-dioxo-, (βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

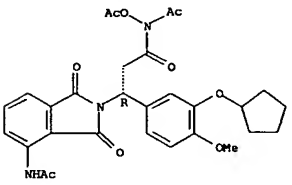


RN 347144-59-6 CAPLUS
CN 2H-Isoindole-2-propanamide, N-acetyl-4-(acetylamino)-N-(acetyloxy)-β-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)



RN 347144-60-9 CAPLUS
CN 2H-Isoindole-2-propanamide, N-acetyl-4-(acetylamino)-N-(acetyloxy)-β-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,3-dihydro-1,3-dioxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

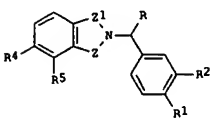


L8 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:359998 CAPLUS
DOCUMENT NUMBER: 134:366799
TITLE: Preparation of isoindolinones for treatment of phosphodiesterase- and TNFα-mediated diseases
INVENTOR(S): Man, Hon-Wah; Muller, George
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034606	A1	20010517	WO 2000-US30770	20001109
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6667316	B1	20031223	US 2000-708199	20001108
CA 2392081	AA	20010517	CA 2000-2392081	20001109
EP 1228071	A1	20020807	EP 2000-977095	20001109
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NZ 519459	A	20031128	NZ 2000-519459	20001109
JP 2004500346	T2	20040108	JP 2001-536553	20001109
NO 2002002223	A	20020708	NO 2002-2223	20020508
FI 2002000892	A	20020510	FI 2002-892	20020510
PRIORITY APPLN. INFO.:			US 1999-165168P	P 19991112
			US 2000-590344	A 20000608
			US 2000-708199	A 20001108
			WO 2000-US30770	W 20001109

OTHER SOURCE(S): MARPAT 134:366799
GI



AB Title compds. [I; R = (CnH2n)R3; R1,R2 = (cyclo)alkyl(oxy), cyano, cycloalkylmethoxy; R3 = hydroxyalkyl, cyano, SO2R6, COR7; 1 of R4,R5 = H and the other = pyrrolyl, imidazolyl, (un)substituted amino(alkyl), etc.; R4,R5 = (un)substituted amino(alkyl); R4R5 = atoms to complete a ring; R6 = alkyl, Ph, CH2Ph; R7 = groups cited for R6, (un)substituted amino; 1 of Z,Z1 = CO or SO2 and the other = CH2, CO, SO2, CH2CO; n = 1-3] were prepared for treatment of phosphodiesterase- and TNFα-mediated diseases (no

L8 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

data). Thus, 3,4-dinitrophthalic acid was cyclocondensed with H2NCH(CH2SO2Me)C6H3(OEt)(OMe)-3,4 and the product reduced to give I (R = CH2SO2Me, R1 = OMe, R2 = OEt, R4 = R5 = NH2, Z = Z1 = CO).

IT **340019-71-8P 340019-72-9P 340019-73-0P 340019-74-1P 340019-75-2P 340019-76-3P 340019-95-6P**

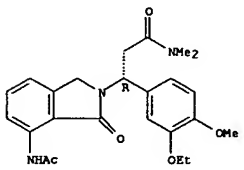
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of isoindolinones for treatment of phosphodiesterase- and TNFα-mediated diseases)

RN 340019-71-8 CAPLUS

CN 2H-Isoindole-2-propanamide, 7-(acetylamino)-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

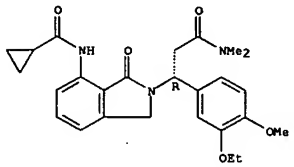
Absolute stereochemistry.



RN 340019-72-9 CAPLUS

CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

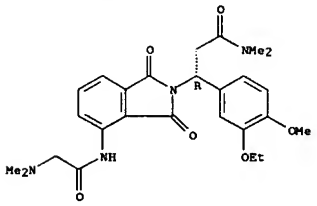
Absolute stereochemistry.



RN 340019-73-0 CAPLUS

CN 2H-Isoindole-2-propanamide, 4-[[(dimethylamino)acetyl]amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1,3-dioxo-, monohydrochloride (9CI) (CA INDEX NAME)

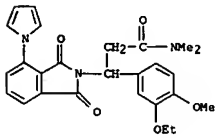
L8 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



● HCl

RN 340019-76-3 CAPLUS

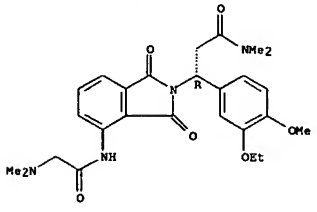
CN 2H-Isoindole-2-propanamide, β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1,3-dioxo-4-(1H-pyrrol-1-yl)- (9CI) (CA INDEX NAME)



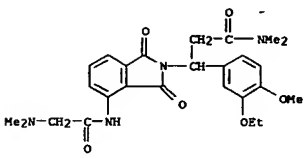
RN 340019-95-6 CAPLUS

CN 2H-Isoindole-2-propanamide, 4-[[(dimethylamino)acetyl]amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1,3-dioxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

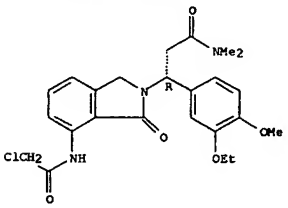


● HCl

RN 340019-74-1 CAPLUS

CN 2H-Isoindole-2-propanamide, 7-[(chloroacetyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 340019-75-2 CAPLUS

CN 2H-Isoindole-2-propanamide, 4-[[(dimethylamino)acetyl]amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1,3-dioxo-, monohydrochloride, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

IT **340020-04-4**

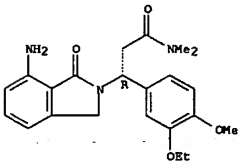
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of isoindolinones for treatment of phosphodiesterase- and TNFα-mediated diseases)

RN 340020-04-4 CAPLUS

CN 2H-Isoindole-2-propanamide, 7-amino-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



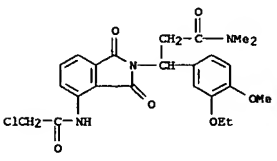
IT **340019-93-4P 340019-94-5P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of isoindolinones for treatment of phosphodiesterase- and TNFα-mediated diseases)

RN 340019-93-4 CAPLUS

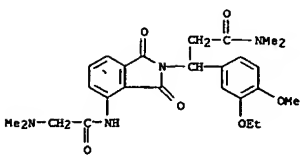
CN 2H-Isoindole-2-propanamide, 4-[(chloroacetyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1,3-dioxo- (9CI) (CA INDEX NAME)



RN 340019-94-5 CAPLUS

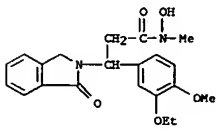
CN 2H-Isoindole-2-propanamide, 4-[[(dimethylamino)acetyl]amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1,3-dioxo- (9CI) (CA INDEX NAME)

L8 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
factor-α levels)
RN 220360-68-9 CAPLUS
CN 2H-Isoindole-2-propanamide, β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N-hydroxy-N-methyl-1-oxo- (9CI) (CA INDEX NAME)

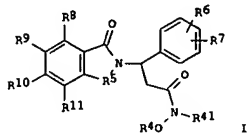


REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:255928 CAPLUS
DOCUMENT NUMBER: 134:280706
TITLE: Preparation of isoindolylhydroxypropionamides for reduction of tumor necrosis factor-α levels.
INVENTOR(S): Muller, George W.; Man, Hon-Wah
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: U.S., 17 pp., Cont.-in-part of U.S. Ser. No. 903,975, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6214857	B1	20010410	US 1998-126157	19980730
TR 200000221	T2	20000921	TR 2000-200000221	19980730
PT 1035848	T	20030930	PT 1998-938151	19980730
ES 2196592	T3	20031216	ES 1998-938151	19980730
MX 200001018	A	20001110	MX 2000-1018	20000128
US 2001049371	A1	20011206	US 2001-780725	20010209
US 6656964	B2	20031202		
US 2004006096	A1	20040108	US 2003-462319	20030616
PRIORITY APPLN. INFO.:			US 1997-903975	B2 19970731
			US 1998-126157	A3 19980730
			US 2000-590344	A3 20000608
			US 2001-780725	A1 20010209

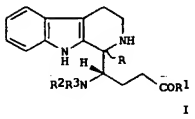
OTHER SOURCE(S): MARPAT 134:280706
GI



I

AB Title compds. e.g., (I; R4, R41 = H, alkyl; R5 = CO, CH2; R6, R7 = NO2, cyano, CF3, EtO2C, MeO2C, Ac, AcO, CO2H, OH, alkyl, etc.; R8-R11 = H, NO2, cyano, CF3, EtO2C, MeO2C, Ac, AcO, CO2H, OH, amino, acylamino, alkyl, etc.), were prepared for reduction of TNF-α levels (no data). Thus, 3-(3-ethoxy-4-methoxyphenyl)-3-(1-oxoisoindolinyl)propanoic acid and carbonyldiimidazole were stirred 2 h in THF; NH2OH.HCl was added and the resulting suspension was stirred 18 h to give 82% 3-(3-ethoxy-4-methoxyphenyl)-N-hydroxy-3-(1-oxoisoindolinyl)propionamide. I drug formulations are given.
IT 220360-68-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of isoindolylhydroxypropionamides for reduction of tumor necrosis

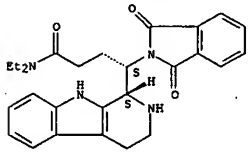
L8 ANSWER 10 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:303576 CAPLUS
DOCUMENT NUMBER: 133:74174
TITLE: Synthesis of tetrahydro-β-carbolines and studies of the Pictet-Spengler reaction
AUTHOR(S): Ducrot, Pierre; Rabhi, Cherif; Thal, Claude
CORPORATE SOURCE: Institut de Chimie des Substances Naturelles, CNRS, Gif-sur-Yvette, 91198, Fr.
SOURCE: Tetrahedron (2000), 56(17), 2683-2692
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 133:74174
GI



I

AB Tetrahydro-β-carbolines I (R = α-, β-H; R1 = OCMe3, R2 = Cbz, Boc, CO2Me, Troc, R3 = H; R1 = OCMe3, R2R3N = pyrrole; R1 = NEt2, R2R3N = phthalimido) have been prepared in a diastereomerically pure form by a short, efficient synthetic sequence consisting of reaction of α-aminoaldehydes with tryptamine. A study was made of the major factors affecting the stereoselectivity of the Pictet-Spengler reaction.
IT 279675-26-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of tetrahydro-β-carbolines via the Pictet-Spengler reaction)
RN 279675-26-2 CAPLUS
CN 1H-Pyrido[3,4-b]indole-1-butanamide, γ-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)-N,N-diethyl-2,3,4,9-tetrahydro-, (γS,1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

L8 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:113548 CAPLUS
DOCUMENT NUMBER: 130:168235
TITLE: Substituted alkanohydroxamic acids and method of reducing TNFα levels
INVENTOR(S): Muller, George W.; Man, Hon-Wah
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9906041	A1	19990211	WO 1998-US15868	19980730
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2295295	AA	19990211	CA 1998-2295295	19980730
AU 9886741	A1	19990222	AU 1998-86741	19980730
AU 737008	B2	20010809		
EP 1035848	A1	20000920	EP 1998-938151	19980730
EP 1035848	B1	20030423		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
TR 200000221	T2	20000921	TR 2000-200000221	19980730
BR 9815895	A	20010116	BR 1998-15895	19980730
JP 2001511448	T2	20010814	JP 2000-504855	19980730
NZ 502379	A	20021025	NZ 1998-502379	19980730
RU 2199530	C2	20030227	RU 2000-102639	19980730
AT 238052	E	20030515	AT 1998-938151	19980730
PT 1035848	T	20030930	PT 1998-938151	19980730
ES 2196592	T3	20031216	ES 1998-938151	19980730
NO 9906529	A	20000328	NO 1999-6529	19991228
FI 2000000061	A	20000302	FI 2000-61	20000112
MX 200001018	A	20001110	MX 2000-1018	20000128

PRIORITY APPLN. INFO.: US 1997-903975 A 19970731
WO 1998-US15868 W 19980730

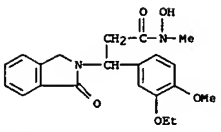
OTHER SOURCE(S): MARPAT 130:168235

AB Ioxoisoindolinylpropionamides and phthalimidopropionamidemidos were prepared and reduce the levels of TNFα and inhibit phosphodiesterase in a mammal. A typical embodiment is 3-(3-cyclopentyloxy-4-methoxyphenyl)-N-hydroxy-3-phthalimidopropionamide which was prepared by the reaction of 3-amino-(3-(3-cyclopentyloxy-4-methoxyphenyl))propionic acid and NH2OH.HCl.

IT 220360-68-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and reduction of TNFα levels and inhibition of phosphodiesterase)

RN 220360-68-9 CAPLUS
CN 2H-Isoindole-2-propanamide, β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N-hydroxy-N-methyl-1-oxo- (9CI) (CA INDEX NAME)

L8 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN

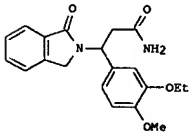
ACCESSION NUMBER: 1998:1310 CAPLUS
DOCUMENT NUMBER: 128:75298
TITLE: Cyclic amides
INVENTOR(S): Muller, George W.
PATENT ASSIGNEE(S): Celgene Corp., USA
SOURCE: U.S., 25 pp., Cont.-in-part of U.S. 5,605,914.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5698579	A	19971216	US 1996-703708	19960827
US 5463063	A	19951031	US 1993-140237	19931020
US 5605914	A	19970225	US 1994-258587	19940610
EP 1004580	A2	20000531	EP 2000-200491	19940701
EP 1004580	A3	20021002		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
EP 1004581	A2	20000531	EP 2000-200492	19940701
EP 1004581	A3	20020814		
EP 1004581	B1	20040922		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
EP 1004572	A2	20000531	EP 2000-200498	19940701
EP 1004572	A3	20021002		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
EP 1477486	A2	20041117	EP 2004-77075	19940701
EP 1477486	A3	20041215		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
US 5877200	A	19990302	US 1997-920715	19970829
US 6075041	A	20000613	US 1998-158612	19980922
US 6200987	B1	20010313	US 2000-547085	20000411
US 2003144325	A1	20030731	US 2003-337602	20030106

PRIORITY APPLN. INFO.:
US 1993-87510 B2 19930702
US 1993-140237 A2 19931020
US 1994-258587 A2 19940610
EP 1994-921439 A3 19940701
EP 2000-200492 A3 19940701
US 1996-703708 A3 19960827
US 1997-920715 A3 19970829
US 1998-158612 A3 19980922
US 1999-230389 A3 19990507
US 2000-543809 A1 20000406
US 2001-781179 A1 20010212

OTHER SOURCE(S): MARPAT 128:75298

GI



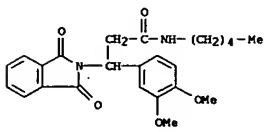
I

AB Cyclic amides such as I are prepared Thus, I was prepared in 2 steps starting
from 3-amino-3-(3-ethoxy-4-methoxyphenyl)propionic acid and phthalaldehyde.

IT **167887-05-0P 167887-06-1P 167887-07-2P**
167887-26-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(cyclic amides as potential tumor necrosis factor inhibitors)

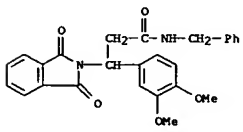
RN 167887-05-0 CAPLUS

CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1,3-dioxo-N-pentyl- (9CI) (CA INDEX NAME)



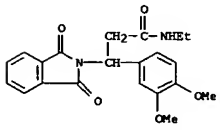
RN 167887-06-1 CAPLUS

CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1,3-dioxo-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



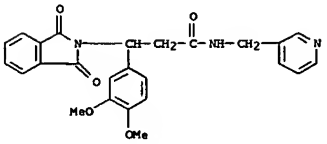
RN 167887-07-2 CAPLUS

CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-N-ethyl-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)

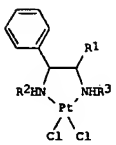


RN 167887-26-5 CAPLUS

CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1,3-dioxo-N-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 1997:679452 CAPLUS
DOCUMENT NUMBER: 127:365319
TITLE: The stereoselectivity of antitumor active [1,2-diamino-1-phenylpropane]dichloroplatinum(II) complexes
AUTHOR(S): Gust, Ronald; Gelbcke, Michael; Angermaier, Bernhard; Bachmann, Helmut; Krauser, Rudolf; Schoenenberger, Helmut
CORPORATE SOURCE: Institut fuer Pharmazie der FU Berlin, 14195, Berlin (Dahlem), Germany
SOURCE: Inorganica Chimica Acta (1997), 264(1-2), 145-160
CODEN: ICHAA3; ISSN: 0020-1693
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

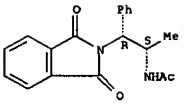
AB The syntheses of enantiomeric threo- and erythro-1,2-diamino-1-phenylpropanes (Ph/Me) and of racemic 1,2-diaminophenylethane (Ph/H) are described. These diamines and related N2-methyl- and N1,N2-dimethyl-1,2-diamino-1-phenylpropanes were transformed into dichloroplatinum(II) complexes I [R1 = R2 = R3 = H (Ph/H-PtCl2); R1 = Me, R2 = R3 = Me (Ph/Me-PtCl2); R1 = R3 = Me, R2 = H (Ph/Me-Me-PtCl2); R1 = R2 = R3 = Me (Ph/Me-Dime-PtCl2)]. For the 1H NMR spectroscopic determination of their optical
purity the diamines (Ph/Me) were converted with (R)-myrtenal into their diimines. In the test on the MCF-7 breast cancer cell line (R,R)-Ph/Me-PtCl2 produced the strongest effect of all new complexes, comparable with that of the standard cisplatin and of other Pt complexes. Its
enantiomer (S,S)-Ph/Me-PtCl2 possessed a distinctly weaker inhibitory potency while the erythro-configurated counterparts were even less active [(R,R)>(S,S)>(S,R) = (R,S)]. All N2-methylated and N1,N2-dimethylated complexes (Ph/Me-Me-PtCl2, Ph/Me-Dime-PtCl2) showed comparable activities equaling those of (R,S)- and (S,R)-Ph/Me-PtCl2. The mol. reasons for the differing potencies of the diastereomeric and enantiomeric Ph/Me-PtCl2 complexes are discussed in consideration of the complex conformation.

IT **198221-71-5P 198221-72-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(for preparation of erythro 1,2-diamino-1-phenylpropane ligand)

RN 198221-71-5 CAPLUS

CN Acetamide, N-[2-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)-1-methyl-2-phenylethyl]-, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

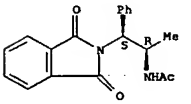
Absolute stereochemistry.



RN 198221-72-6 CAPLUS

CN Acetamide, N-[2-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)-1-methyl-2-phenylethyl]-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN

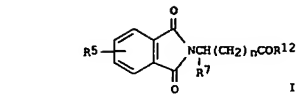
ACCESSION NUMBER: 1997:169160 CAPLUS
DOCUMENT NUMBER: 126:199454
TITLE: Preparation of cyclic imides as inhibitors of tumor necrosis factor α
INVENTOR(S): Muller, George W.
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: U.S., 22 pp., Cont.-in-part of U.S. Ser. No. 87,510, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5605914	A	19970225	US 1994-258587	19940610
US 5463063	A	19951031	US 1993-140237	19931020
EP 1004580	A2	20000531	EP 2000-200491	19940701
EP 1004580	A3	20021002		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
EP 1004581	A2	20000531	EP 2000-200492	19940701
EP 1004581	A3	20020814		
EP 1004581	B1	20040922		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
EP 1004572	A2	20000531	EP 2000-200498	19940701
EP 1004572	A3	20021002		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
EP 1477486	A2	20041117	EP 2004-77075	19940701
EP 1477486	A3	20041215		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
US 5698579	A	19971216	US 1996-703708	19960827
US 5877200	A	19990302	US 1997-920715	19970829
US 6075041	A	20000613	US 1998-158612	19980922
US 6200987	B1	20010313	US 2000-547085	20000411
US 2003144325	A1	20030731	US 2003-337602	20030106

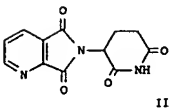
PRIORITY APPLN. INFO.:
US 1993-87510 B2 19930702
US 1993-140237 A2 19931020
US 1994-258587 A2 19940610
EP 1994-921439 A3 19940701
EP 2000-200492 A3 19940701
US 1996-703708 A3 19960827
US 1997-920715 A3 19970829
US 1998-158612 A3 19980922
US 1999-230389 A3 19990507
US 2000-543809 A1 20000406
US 2001-781179 A1 20010212

GI

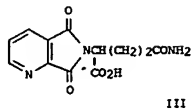
L8 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



I



II

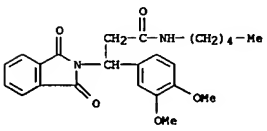


III

AB Cyclic imides, such as I [R5 = H, NO2, CN, CF3, CO2Et, CO2Me, CO2Pr, Ac, CONH2, AcO, CO2H, OH, NH2, alkyl, alkoxy, halo; R7 = pyridyl, substituted Ph, (un)substituted benzyl, naphthyl, benzyloxy, imidazol-4-ylmethyl; R12 = amino, OH, ester; n = 0-3], are inhibitors of tumor necrosis factor α and can be used to combat cachexia, endotoxic shock, and retrovirus replication. Thus, I (R5 = H, R7 = 4-MeOC6H4, R12 = NH2, n = 1) was prepared from 3-(4-MeOC6H4)CH(NH2)CH2CO2H and N-(carboethoxy)phthalimide via amidation of the phthalimidopropionic acid. Also, 2-(2,6-dioxo-3-piperidinyl)-4-azaisoindoline-1,3-dione (II) was prepared from L-glutamine and 2,3-pyridinedicarboxylic anhydride via intramol. cyclization of glutaramic acid III.

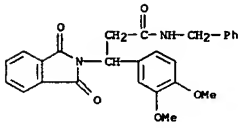
IT 167887-05-0P 167887-06-1P 167887-07-2P
167887-26-5P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cyclic imides as inhibitors of tumor necrosis factor α)

RN 167887-05-0 CAPLUS
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1,3-dioxo-N-pentyl- (9CI) (CA INDEX NAME)

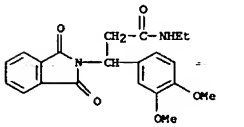


RN 167887-06-1 CAPLUS
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1,3-dioxo-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

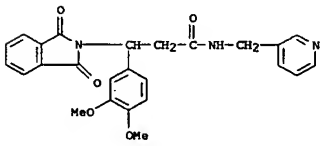
L8 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 167887-07-2 CAPLUS
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-N-ethyl-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)

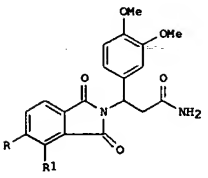


RN 167887-26-5 CAPLUS
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1,3-dioxo-N-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



L8 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:452533 CAPLUS
DOCUMENT NUMBER: 125:157753
TITLE: Structural Modifications of Thalidomide Produce Analogs with Enhanced Tumor Necrosis Factor Inhibitory Activity
AUTHOR(S): Muller, George W.; Corral, Laura G.; Shire, Mary G.; Wang, Hua; Moreira, Andre; Kaplan, Gilla; Stirling, David I.
CORPORATE SOURCE: Celgene Corporation, Warren, NJ, 07059, USA
SOURCE: Journal of Medicinal Chemistry (1996), 39(17), 3238-3240
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



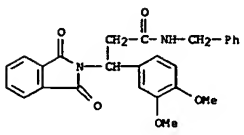
I

AB Thalidomide (α-N-phthalimidoglutarimide) has been shown to have a wide range of varied biol. activities, including the ability to inhibit tumor necrosis factor-α (TNF-α) production and its accompanying inflammatory manifestations. The central role of TNF-α as a pro-inflammatory cytokine of the immune response suggests that the drug may have important therapeutic utility in a variety of diseases including acute and chronic infections, auto-immune disorders, and malignancies. To prepare a family of drugs with increased anti-TNF-α activity, a series of analogs of thalidomide was designed, synthesized, and tested for their ability to inhibit TNF-α release by peripheral blood mononuclear cells in vitro. A series of N-phthaloyl β-amino-β-aryl amides and esters was found to have increased activity in inhibiting TNF-α production The more potent analogs reported here, compds. (I, R = H, R1 = NH2) and (II, R = NH2, R1 = H) are 400-500 times more active than thalidomide in inhibiting TNF-α production

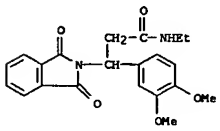
IT 167887-06-1 167887-07-2 180266-91-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(thalidomide analog preparation for compds. with enhanced TNF-α inhibitory activity)

RN 167887-06-1 CAPLUS
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1,3-dioxo-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

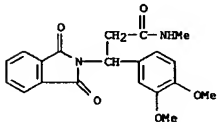
L8 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 167887-07-2 CAPLUS
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-N-ethyl-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)



RN 180266-91-5 CAPLUS
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-N-methyl-1,3-dioxo- (9CI) (CA INDEX NAME)



L8 ANSWER 16 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1995:797249 CAPLUS
DOCUMENT NUMBER: 123:198617
TITLE: Imides as inhibitors of TNF alpha
INVENTOR(S): Muller, George W.
PATENT ASSIGNEE(S): Celgene Corp., USA
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9501348	A2	19950112	WO 1994-US7411	19940701
WO 9501348	A3	19950309		
W: AU, CA, CZ, FI, HU, JP, KR, NZ, PL, RU, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2166315	AA	19950112	CA 1994-2166315	19940701
AU 9472167	A1	19950124	AU 1994-72167	19940701
AU 687843	B2	19980305		
EP 706521	A1	19960417	EP 1994-921439	19940701
EP 706521	B1	20021002		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09500872	T2	19970128	JP 1994-503648	19940701
HU 75312	A2	19970528	HU 1996-3	19940701
EP 1004580	A2	20000531	EP 2000-200491	19940701
EP 1004580	A3	20021002		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
EP 1004581	A2	20000531	EP 2000-200492	19940701
EP 1004581	A3	20020814		
EP 1004581	B1	20040922		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
EP 1004572	A2	20000531	EP 2000-200498	19940701
EP 1004572	A3	20021002		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
PL 180377	B1	20010131	PL 1994-312386	19940701
RU 2174516	C2	20011010	RU 1996-102001	19940701
AT 225344	E	20021015	AT 1994-921439	19940701
PT 706521	T	20030228	PT 1994-921439	19940701
ES 2184765	T3	20030416	ES 1994-921439	19940701
AT 277036	E	20041015	AT 2000-200492	19940701
EP 1477486	A2	20041117	EP 2004-77075	19940701
EP 1477486	A3	20041215		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
CZ 294444	B6	20050112	CZ 2003-663	19940701
FI 9506362	A	19960226	FI 1995-6362	19951229
US 6476052	B1	20021105	US 2000-633908	20000807
US 2003144325	A1	20030731	US 2003-337602	20030106
FI 2004000593	A	20040427	FI 2004-593	20040427

PRIORITY APPLN. INFO.:

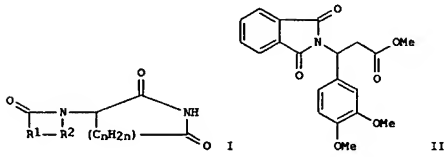
US 1993-87510	A	19930702
EP 1994-921439	A3	19940701
EP 2000-200492	A3	19940701
WO 1994-US7411	W	19940701
US 1996-690258	A1	19960724
US 1996-701494	A1	19960822
US 1997-48278P	P	19970530
WO 1997-US13375	A1	19970724
US 1999-230389	B3	19990507
US 2000-543809	A1	20000406

L8 ANSWER 16 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

US 2001-781179 A1 20010212

OTHER SOURCE(S): MARPAT 123:198617

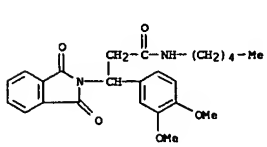
GI



AB A variety of cyclic imides and certain acyclic analogs and/or precursors are inhibitors of tumor necrosis factor α (no data) and can be used to combat cachexia, endotoxic shock, and retrovirus replication. One subgroup of the compds. is I [R1 = divalent residue of 3,4-pyridine, pyrrolidine, imidazole, naphthalene, thiophene, or C2-6 alkane (un)substituted by (un)substituted Ph; R2 = CO, SO2; n = 1-3]. A typical embodiment from a different subgroup is Me 3-phthalimido-3-(3,4-dimethoxyphenyl)propionate, i.e. II, which was prepared from 3,4-(MeO)2C6H3CH(NH2)CH2CO2H by conversion to the Me ester hydrochloride with SOCl2 and MeOH (66%) and reaction of this with N-(carboethoxy)phthalimide in the presence of Na2CO3 in aqueous MeCN (92%). A total of 93 synthetic examples and 6 formulations are given.

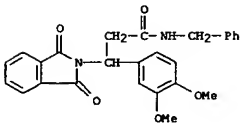
IT 167887-05-0P 167887-06-1P 167887-07-2P 167887-26-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cyclic imides and analogs as TNF-α inhibitors)

RN 167887-05-0 CAPLUS
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1,3-dioxo-N-pentyl- (9CI) (CA INDEX NAME)

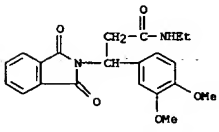


RN 167887-06-1 CAPLUS
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1,3-dioxo-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

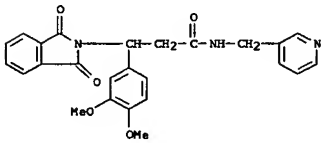
L8 ANSWER 16 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 167887-07-2 CAPLUS
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-N-ethyl-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)

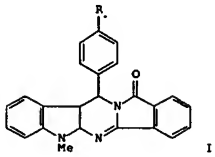


RN 167887-26-5 CAPLUS
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1,3-dioxo-N-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



L8 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1982:562930 CAPLUS
DOCUMENT NUMBER: 97:162930
TITLE: Intramolecular cyclization of N-phthalyl-β-aryl-β-alanine phenylhydrazide
AUTHOR(S): Portnov, Yu. N.; Zabrodnyaya, V. G.; Voronin, V. G.; Kost, A. N.
CORPORATE SOURCE: Vses. Nauchno-Issled. Khim.-Farm. Inst., Kupavna, 142450, USSR
SOURCE: Khimiya Geterotsiklicheskikh Soedinenii (1982), (7), 926-9
CODEN: KGSSAQ; ISSN: 0453-8234
DOCUMENT TYPE: Journal
LANGUAGE: Russian
OTHER SOURCE(S): CASREACT 97:162930
GI

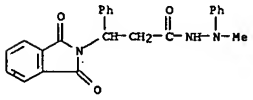


I

AB Reaction of the N'-methyl-N'-phenylhydrazides of N-phthalyl-β-aryl-β-anilines with POCl3 initially gave indolimines (isolable at lower reaction temperature), which cyclized further to give I (R = H, MeO).

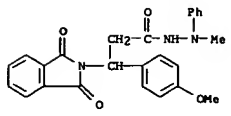
IT 83256-53-5P 83256-54-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of)

RN 83256-53-5 CAPLUS
CN 2H-Isoindole-2-propanoic acid, 1,3-dihydro-1,3-dioxo-β-phenyl-, 2-methyl-2-phenylhydrazide (9CI) (CA INDEX NAME)



RN 83256-54-6 CAPLUS
CN 2H-Isoindole-2-propanoic acid, 1,3-dihydro-β-(4-methoxyphenyl)-1,3-dioxo-, 2-methyl-2-phenylhydrazide (9CI) (CA INDEX NAME)

L8 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



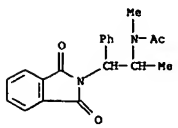
L8 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1968:506661 CAPLUS
DOCUMENT NUMBER: 69:106661
TITLE: Condensation reaction of aminoalkyl esters with imides
AUTHOR(S): Nakajima, Kazuo; Shinuchi, Takami; Tauchi, Miyako
CORPORATE SOURCE: Teikoku Chem. Ind., Kyoto, Japan
SOURCE: Nippon Kagaku Zasshi (1968), 89(4), 408-11
CODEN: NPKZAZ; ISSN: 0369-5387
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB H2NCH2CH2NHCH2CH2OH (104 g.) treated with 337 g. Ac2O and heated with 147 g. phthalimide (I) after removal of AcOH, 70 g. PhAc being added to keep the temperature at 220-40° and AcOH being removed, gave after hydrolysis 70 g. (H2NCH2CH2)2NH, b. 207°. Similarly, PhNHCH2CH2NHCH2CH2NH2, b11 183-5°, was obtained in 75% yield. The similar reaction was applied to polyfunctional compds. The following new compds. were prepared (compound, m.p., b6 and % yield given): C6H11N(CH2CH2OAc)2 (C6H11 = cyclohexyl), -, 161°, 97; PhN(CH2CH2OAc)2, -, 186°, 94; C6H4(CO)2NCH2CH2NMeCH2CH2OAc [C6H4(CO)2N = phthalimido], -, 206°, 60; C6H4(CO)2NCH2CH2N(C6H11)CH2CH2OAc, 56°, 246°, 58; C6H4(CO)2NCH2CH2NPhCH2CH2OAc, 105°, decompose, 61; MeN[CH2CH2N(CO)2C6H4]2, 126°, 290°, 85; C6H11N[CH2CH2N(CO)2C6H4]2, 125°, 304°, 87; PhN[CH2CH2N(CO)2C6H4]2, 213°, decompose, 85; H2NCH2CH2N(C6H11)CH2CH2OH, -, 147°, 80; H2NCH2CH2NPhCH2CH2OH, 42°, 171°, 85; C6H11N(CH2CH2NH2)2 (II), -, 125°, 80; PhN(CH2CH2NH2)2 (III), -, 157°, 80. Chloroplatinate of II and picrate of III melt at 230° and 210°, resp. N,N'-Bis(2-hydroxyethyl)piperazine gave diacetate (IV), b10 177-80° (picrate, m. 242°), which was treated with 1 mole I to give 30% N-2-acetoxyethyl-N'-2-phthalimidoethylpiperazine, b7 168-70°; picrate m. 248°. Hydrolysis gave N-2-hydroxyethyl-N'-2-aminoethylpiperazine, b15 168°; picrate, m. 149°. Treating IV with 2 moles I gave N,N'-bis(2-phthalimidoethyl)piperazine, m. 234° (picrate decomposition p. 299°), whose hydrolysis yielded N,N'-bis(2-aminoethyl)piperazine, b. 267°; picrate m. 206°. Treating l-ephedrine with Ac2O followed by I gave C6H4(CO)2NCHPhCHMeNMeAc, m. 145°, b6 234°, whose hydrolysis yielded PhCH(NH2)CHMeNHMe, b. 246°; picrate m. 166°; HCl salt decomposition p. 264°. Treating Et2N(CH2)3OH with (EtCO)2O yielded Et2N(CH2)3O2CEt, b. 235-7°, which was treated with I to give Et2N(CH2)3N(CO)2C6H4, b6 185°. Hydrolysis gave Et2N(CH2)3NH2, b. 169°; picrate m. 196°.

IT 20542-02-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 20542-02-3 CAPLUS
CN Acetamide, N-methyl-N-(α-methyl-β-phthalimidophenethyl)- (8CI) (CA INDEX NAME)



L8 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

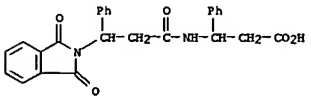
L8 ANSWER 19 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1968:487466 CAPLUS
DOCUMENT NUMBER: 69:87466
TITLE: Synthesis of dipeptides of some β-amino acids via α-diazo ketones
AUTHOR(S): Jugelt, W.; Falck, P.
CORPORATE SOURCE: Humboldt-Univ. Berlin, Berlin, Fed. Rep. Ger.
SOURCE: Journal fuer Praktische Chemie (Leipzig) (1968), 38(1-2), 88-100
CODEN: JPCEAO; ISSN: 0021-8383
DOCUMENT TYPE: Journal
LANGUAGE: German
OTHER SOURCE(S): CASREACT 69:87466

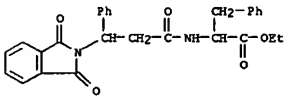
AB The Wolff rearrangement of 1-phthaloylamino-3-diazo-2-alkanones in the presence of DL-H2NCHPhCH2CO3Et or DL-phenylalanine esters, catalyzed by Ag2O, or occurring photolytically, yielded β-phthaloylaminopropionyl-amino acid esters, which upon saponification of the ester group and subsequent hydrazinolysis gave the following H3N+CHRCHR1C(O)NHCHR2(CH2)nCO2- (R = H or Ph, R1 = H, Me, Et and R2 = Ph or CH2Ph, n = 0 or 1).

IT **19745-62-1P 19745-75-6P 19771-39-2P**
19771-62-1P 19776-44-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 19745-62-1 CAPLUS
CN Hydrocinnamic acid, β-(β-phthalimidohydrocinnamamido)- (8CI) (CA INDEX NAME)

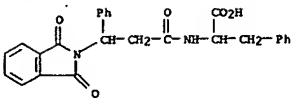


RN 19745-75-6 CAPLUS
CN Alanine, 3-phenyl-N-(β-phthalimidohydrocinnamoyl)-, ethyl ester, DL- (8CI) (CA INDEX NAME)

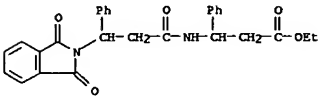


RN 19771-39-2 CAPLUS
CN Alanine, 3-phenyl-N-(β-phthalimidohydrocinnamoyl)-, DL- (8CI) (CA INDEX NAME)

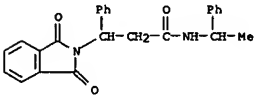
L8 ANSWER 19 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 19771-62-1 CAPLUS
CN Hydrocinnamic acid, β-(β-phthalimidohydrocinnamamido)-, ethyl ester (8CI) (CA INDEX NAME)



RN 19776-44-4 CAPLUS
CN 2-Isoindolinepropionamide, N-(α-methylbenzyl)-1,3-dioxo-β-phenyl- (8CI) (CA INDEX NAME)



L8 ANSWER 20 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1968:477009 CAPLUS
DOCUMENT NUMBER: 69:77009
TITLE: Tetracyclines. XLVII. Derivatives of (4-oxto-5,10-dihydroxy-9-methyl-1,2,3,4-tetrahydro-2-anthryl)glycine
AUTHOR(S): Gurevich, A. I.; Karapetyan, M. G.; Kolosov, M. N.; Korobko, V. G.; Onoprienko, V. V.; Popravko, S. A.
CORPORATE SOURCE: Inst. Khim. Prir. Soedin., Moscow, USSR
SOURCE: Zhurnal Obshchei Khimii (1968), 38(1), 50-7
CODEN: ZOKHA4; ISSN: 0044-460X
DOCUMENT TYPE: Journal
LANGUAGE: Russian

GI For diagram(s), see printed CA Issue.

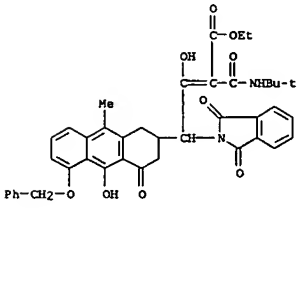
AB The following intermediates for synthesis of tetracycline were reported. I stirred 2 hrs. with Zn dust in AcOH at room temperature gave 78% Et 4-oxo-5-benzyloxy-10-hydroxy-9-methyl-1,2,3,4-tetrahydro-2-anthryloximinoacetate, m. 126-7°. Similar reduction with activated Zn dust (10 parts by weight) gave 74% 2-(4-oxo-5-benzyloxy-10-hydroxy-9-methyl-1,2,3,4-tetrahydro- 2-anthryl)glycine Et ester (II), m. 138-40°, while reduction at 40° in 3 hrs. gave 53% above ester and 15% 2-(5-benzyloxy-4,10-dihydroxy-9-methyl-1,2,3,4-tetrahydro-2-anthryl)glycine, m. 99-101°. II and MeI in tetrahydrofuran (THF) 18 hrs. gave 18% Et ester of 2-(4-oxo-5-benzyloxy-10-hydroxy-9-methyl-1,2,3,4-tetrahydro-2-anthryl)sarcosine (III), m. 144-6°, and 18% corresponding N,N-dimethylglycine analog (IV), m. 149-51°. The latter was formed in 59% yield from this reaction in Me2NCHO in the presence of Ag2O, while treating II with 4% formalin in THF at 0°, followed by NaBH4 at 0-2° 3 hrs. gave 46% III. II and Ac2O gave the N-acetyl derivative (V), m. 188-90°, after brief heating. III and Ac2O after refluxing 10 min. also gave the N-acetyl derivative, m. 123-4°. II and phthalic anhydride in THF in 0.5 hr. gave N-o-carboxybenzoyl derivative, m. 154-6°, while II and N-carbethoxyphthalimide in THF gave in 0.5 hr. N-phthaloyl derivative, m. 176-8°, also formed from II and phthalic anhydride after 0.5 hr. at 160°. II and 0.3N KOH THF gave in 2.5 hrs. at 20° 74% 2-(4-oxo-5-benzyloxy-10-hydroxy-9-methyl-1,2,3,4-tetrahydro-2-anthryl)glycine, m. 187-9°; IV heated with alc. KOH 1 hr., neutralized with HCl, diluted with EtOH, evaporated, and kept 12 hrs. in THF at 0° gave 87% 2-(4-oxo-5-benzyloxy-10-hydroxy-9-methyl-1,2,3,4-tetrahydro - 2 - anthryl) - N,N - dimethylglycine, m. 173-80° (decomposition). II and KOH under similar conditions gave, after heating the crude product with Ac2O in the cold 63% 2-(4-oxo-5-benzyloxy-10-hydroxy-9-methyl-1,2,3,4-tetrahydro-2-anthryl)-N-acetylglycine (VI), m. 222-4°, also formed by saponification of V with KOH at 20°. N-Ac derivative of III and KOH in THF at 20° 4 hrs. gave 83% 2-(4-oxo-5-benzyloxy-10-hydroxy-9-methyl-1,2,3,4-tetrahydro - 2 - anthryl) - N - acetylsarcosine, m. 202-4°. II and phthalic anhydride in THF 0.3 hr. at 20°, then treated with 0.36N KOH and kept 3 hrs. longer gave 55% 2-(4-oxo-5-benzyloxy-10-hydroxy-9-methyl-1,2,3,4-tetrahydro-2-anthryl)-N-(o-carboxybenzoyl)glycine, m. 173-5°. The same formed similar saponification of the Et esters of either phthaloyl or carboxybenzoyl analogs. The product heated in diglyme at 140° 1.5 hrs. gave 41% 2-(4-oxo-5-benzyloxy-10-hydroxy-9-methyl-1,2,3,4-tetrahydro-2-anthryl)-N-phthaloylglycine (VII), m. 205-7°. VI and Et3N in THF treated at -70° with COCl2 in MePh 0.5 hr., followed by solution of ethoxymagnesium derivative of Et malonamate in THF, gave after 2 hrs. at room

L8 ANSWER 20 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

temp., followed by an aq. treatment, 41% Et 2-(4-oxo-5-benzyloxy-10-hydroxy-9-methyl-1,2,3,4-tetrahydro-2-anthryl)-N - acetylglycylmalonamate (VIII), m. 157-61°; similarly was prepd. 21% Et 2-(4-oxo-5-benzyloxy-10-hydroxy-9-methyl-1,2,3,4-tetrahydro-2-anthryl)-N-acetylsarcosylmalonamate characterized by ir spectrum. VII similarly gave Et 2-(4-oxo-5-benzyloxy-10-hydroxy-9-methyl- 1,2,3,4 - tetrahydro - 2 - anthryl) - N - phthaloylglycylmalonamate, decompd. 143-8°. Similar reaction of VII with COCl2, followed by ethoxymagnesium deriv. of Et N-tert-butylmalonamate, gave 37% Et [2-(4-oxo-5-benzyloxy-10-hydroxy-9-methyl-1,2,3,4-tetrahydro-2-anthryl)-N-phthaloylglycyl]-N - tert-butylmalonamate, characterized by ir spectrum. VIII and NaH in Me2SO finally at 120° gave 59% 1-acetyl-2-(4-oxo-5-benzyloxy-10-hydroxy-9-methyl-1,2,3,4-tetrahydro-2-anthryl)-4-carbamoyl-3-pyrrolinol-5-one, m. 163-8°.

IT **19638-85-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 19638-85-8 CAPLUS
CN Malonamic acid, 2-[2-[5-(benzyloxy)-1,2,3,4-tetrahydro-10-hydroxy-9-methyl-4-oxo-2-anthryl]-1-hydroxy-2-phthalimidoethylidene]-N-tert-butyl-, ethyl ester (8CI) (CA INDEX NAME)



L8 ANSWER 21 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1966:490458 CAPLUS
DOCUMENT NUMBER: 65:90458
ORIGINAL REFERENCE NO.: 65:16910h,16911a-h,16912a-h,16913a-e,16914a
TITLE: Substituted aminocarboxylic acid derivatives
INVENTOR(S): Crook, Leonard R.; Jansen, Alexander B. A.; Spencer, Kenneth E. V.; Watson, David H.
PATENT ASSIGNEE(S): John Wyeth & Brother Ltd.
SOURCE: 37 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 1036694		19660720	GB	19640303

AB The title compds. (I) are hypnotics, sedatives, muscle relaxants, or anti-convulsants. A mixture of 14.3 g. tetrachlorophthalic anhydride and 5.2 g. NH2(CH2)3CO2H (II) was heated 3 hrs. at 160-80°, cooled, and extracted with boiling AcOH to give 14 g. I (R = H, R1 = R2 = R3 = R4 = Cl, n = 2, X = OH) (Ia), m. 273-5° (ethylene glycol monoethyl ether). Ia (2 g.) was refluxed 1.5 hrs. with SOCl2 to give I (R = H, R1 = R2 = R3 = R4 = Cl, n = 2, X = Cl)(Ib), m. 165-6°. A solution of 3.9 g. Ib in 35 cc. EtOH was treated dropwise with 2 cc. C5H5N to give 3 g. I (R = H, R1 = R2 = R3 = R4 = Cl, n = 2, X = OEt), m. 125.5° (EtOH). A suspension of 19.8 g. 4-amino-4-phenylbutyric acid monohydrate and 14.8 g. phthalic anhydride in 600 ml. PhMe and 25 ml. Et3N was refluxed in a Dean-Stark apparatus for 4 hrs. to give I (R = Ph, R1 = R2 = R3 = R4 = H, n = 2, X = OH), m. 167° (50% aqueous EtOH). Cl(CH2)3CO2Et (1.7 g.) was added to a suspension of 3.2 g. K 3,6-dimethoxyphthalimide in 15 ml. HCONMe2, refluxed 2 hrs., and worked up to give I (R = H, R1 = MeO, R2 = R3 = H, R4 = MeO, n = 2, X = OEt), m. 92-4°. Similarly 1 g. phthaloylglycyl chloride in dioxane reacted with 1.84 g. II in the presence of 0.26 g. Mg(OH)2 and 10 ml. H2O to give 4-(phthalylglycyl)aminobutyric acid (III) m. 217.5-20.5°. A mixture of 3 g. III, 10 ml. absolute EtOH, and 10 ml. concentrated H2SO4 was heated 5 min. on the steam bath to give 2.7 g. ethyl 4-(phthalylglycyl)aminobutyrate, m. 184-5°. A solution of 1.8 g. Ic (see below) in 30 ml. EtOH and 60 ml. EtOAc was hydrogenated in the presence of 0.5 g. 10% Pd-C at 1 atmospheric for 1 hr. to give I (R = R1 = H, R2 = NH2, R3 = R4 = H, n = 2, X = OEt), m. 73-4° (aqueous EtOH). A mixture of 2.75g. IV (see below) in 20 ml. dry EtOH was treated with 3.1 g. EtI and a solution of 0.8 g. NaOH in 15 ml. EtOH and refluxed 8 hrs. to give ethyl 4-(4,4-diethylhomophthalimido)butyrate, b0.3 154-5°, n22.5D 1.5259. A solution of 3.8 g. Id (see below) in AcOH was reduced as above to give I (R = H, R1 = AcNH, R2 = R3 = R4 = H, n = 2, X = OEt), m. 54-5°. A solution of 21.4 g. 1,2,3,4-tetrahydro-2,4-dioxoquinazoline (referred to as benzoyleneurea) and 5.35 g. NaOH in 600 ml. 50% aqueous EtOH was treated with 27 g. Br(CH2)3CN and refluxed 40 hrs. The solvent was distilled and the residue treated with 600 ml. 0.5N NaOH until strongly alkaline
The insol. residue was filtered off and crystallized from EtOH to give 3.5 g.
1,3-bis(3-cyanopropyl)benzoyleneurea, m. 120-2°. The filtrate was adjusted to pH 10 with concentrated HCl to give 12.4 g. 3-(3-cyanopropyl)benzoyleneurea (V), m. 181-2°. Dry HCl was passed for 3 hrs. into a solution of 5.8 g. V in 50 ml. EtOH and then refluxed 20 hrs. to give 4 g. ethyl 4(1,2,3,4-tetrahydro-2,4-dioxo-3-quinoazolinyl)butyrate

L8 ANSWER 21 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

[also referred to as 3-(3-carbethoxypropyl)benzoyleneurea], m. 134-4.5°. A mixt. of 30 g. γ-phthalimidobutyric acid in 200 ml. dry C6H6 and 60 ml. SOCl2 was refluxed 3 hrs., concd. to dryness, the solid residue dissolved in 150 ml. C6H6, and treated with a soln. of 19 g. Et2NH in 50 ml. C6H6 to give I (R = R1 = R2 = R3 = R4 = H, n = 2, X = NEt2), m. 81-2° (aq. EtOH). Levulinic acid (250 g.) was reductively aminated with ice cold NH3 (d. 0.88) and then hydrogenated with 10-20 g. Raney Ni at 100 atm. and 150° to give 5-methyl-2-pyrrolidone, which was then hydrolyzed with Ba(OH)2 under reflux to give 4-aminovaleric acid. A mixt. of 172 g. methyl valerate, 430 ml. MeCH2NO2, and 140 ml. Me3N was kept 4 days at 30° to give methyl 4-nitrovalerate b0.5 74-6°, which was hydrogenated at 3 atm. in the presence of Raney Ni to give 5-methyl-2-pyrrolidinone. A mixt. of 78.3 g. N,N-dimethyl-4-chlorovaleramide (VI) and 116 g. dry Na saccharin in HCONMe2 was refluxed 15 hrs. and worked up to give 2-(1-dimethylaminocarbonylbut-3-yl)-1,1-dioxo-4,5-benzisothiazolin-3-one, m. 106.5-7.0°. In the examples given below the residue 1,1-dioxo-4,5-benzisothiazolin-3-one is referred to as sulfobenzimide. A soln. of 140 g. methyl 4-nitrohexanoate in 200 ml. EtOH was hydrogenated at 60° and 80 atm. for 24 hrs. with 15 g. Raney Ni to give 47.8 g. 5-ethyl-2-pyrrolidinone (VII), b60-100 160-200°, n22D 1.4707. A mixt. of 6.05 g. VII and 9.24 g. Ba(OH)2·H2O in 50 ml. H2O was refluxed 1 hr., treated with 50 ml. H2O and a stream of CO2 until neutral to give 4-aminohexanoic acid. A mixt. of 10.4 g. γ-chlorobutyronitrile and 20.5 g. anhyd. saccharin was heated 2.5 hrs. at 150-80° to give 18 g. of nitrile product, m. 104°. A mixt. of 5 g. of this nitrile and 10 ml. concd. H2SO4 was heated 10 min. on the steam bath to give 2-(1-aminocarbonylprop-3-yl)sulfobenzimide (VIII), m. 151-3° (H2O). A mixt. of 1 g. VIII, 20 ml. Me2CO, 20 ml. H2O, and 5 ml. concd. HCl was refluxed 2 hrs. to give 2-(1-carboxyprop-3yl)sulfobenzimide (IX), m. 106-8° (50% AcOH). IX was converted as above to 2-(1-dimethylaminocarbonylprop-3-yl)sulfobenzimide, m. 84-5°. 1,4-Methano-1,2,3,4-tetrahydronaphthalene-2,3-dicarboxylic anhydride (4.3 g.) was added in small portions over 1 hr. to a stirred soln. of aq. NH3 (d. 0.88) and worked up to give 2 g. of the corresponding imide, m. 242-4°. The K salt of the latter was prepd. by treating a soln. of 2.13 g. of the imide in 55 ml. Me2CO at 50° with alc.-KOH (11.8 ml., 0.845N). A mixt. of 7.53 g. of this K salt and 6 g. N,N-dimethyl 4- chlorobutyramide, n20D 1.4723 (prepd. by treating 100 g. 4-chlorobutyryl chloride in 250 ml. dry Et2O with Me2NH in Et2O until just alk.) in 100 ml. HCONMe2 was refluxed 3.5 hrs. to give 4 g. 1,3-dioxo-2-(3-dimethylaminocarbonylprop-1-yl)-4,9-methano-3a,4,9,9a-tetrahydrobenz[f]isoindoline, m. 118-19°. Zn wool (53 g.) was amalgamated with a soln. of 4.5 g. HgCl2 in 100 ml. H2O and 8 ml. concd. HCl. The liquid was decanted and replaced by 110 ml. H2O and treated with 3.2 g. 4-phthalimidovaleric acid and 52 ml. concd. HCl and heated 3 hrs. on the steam bath to give 4-phthalimidovaleric acid (X), m. 109-9.5°. X (3.24 g.) was converted by the mixed anhydride method using 1.92 ml. Et3N, 1.8 ml. isobutylchloroformate, and 1.1 ml. Me2NH to give N,N-dimethyl-4-phthalimidovaleramide (I, R = Me, R1 = R2 = R3 = R4 = H, n = 2, X = NMe2), m. 81.52.5°. A mixt. of 20.2 g. pent-2-enoic acid, 35.0 g. N-bromosuccinimide, and 100 mg. Bz2O2 in 200 cc. CCl4 was refluxed 4 hrs. to give 4-bromopent-2-enoic acid, m. 78-80°. Valerolactone was heated with SOCl2 and freshly fused ZnCl2 at 100° for 70 hrs. to give 4-chlorovaleryl chloride, which was treated with an ethereal soln. of Me2NH to give VI, b30 45-81°. A mixt. of 50 g. β,β-dimethylacrylic acid and 700 ml. concd. NH3 was heated 32 hrs. in an autoclave at 150° and worked up to give 30.5 g. 3-amino-3-methylbutyric acid, m. 218-21° (sealed tube). A soln. of 3-methyl-3-phthalimidobutyryl chloride, m. 78-9.5°, in 25

L8 ANSWER 21 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

ml. dry C6H6 was added to a soln. of 120 ml. Et2O contg. 2.2 equivs. of CH2N2 to give 4.55 g. of the diazo ketone. This was dissolved in 100 ml. dioxane and added to a stirred mixt. of 1.5 g. Na2S2O3·5H2O and 1.5 g. AgO in 250 ml. H2O in a bath at 5565°. The mixt. was stirred 7 hrs. to give 4-methyl-4-phthalimidovaleric acid, m. 134.5-6°. A mixt. of 100 g. K phthalimide, 54.5 g. redistd. γ-butyrolactone, and 270 ml. HCONMe2 was refluxed 15 hrs., cooled, poured onto 600 g. ice, and treated with 50 ml. concd. HCl to give I (R = R1 = R2 = R3 = R4 = H, n = 2, X = OH), m. 117-18° (aq. EtOH). Me2SO4 (30 ml.) was added to a soln. of 10 g. 3,6-dihydroxyphthalonitrile in 150 ml. Me2CO. NaOH soln. (2N, 150 ml.) was added in portions over 15 min., the soln. refluxed 1 hr., and cooled overnight to give 3,6-diethoxyphthalonitrile, m. 197-200°. The nitrile was refluxed 6 hrs. with a mixt. of 24 ml. 5N NaOH and 80 ml. H2O to give 3,6-diethoxyphthalic anhydride, m. 202-3° (AcOH). The following I derivs. were similarly prepd. by the various procedures given above (R, R1, R2, R3, R4, n, X, and m.p. given): Ph, H, H, H, H, 2, OEt, 71°; H, Ph, H, H, Ph, 2, OH, 186.58.0°; H, Ph, H, H, Ph, 2, OEt, 130-1°; H, Me, H, H, Me, 2, OH, 195-6.5°; H, Me, H, H, Me, 2, OEt, 57-8°; H, H, NO2, H, H, 2, OEt (Ic), 67-9°; H, NO2, H, H, H, 2, OH, 134-4.5°; H, NO2, H, H, H, 2, OEt (Id), 51-2°; H, H, H, H, H, 3, OH, 156-8°; H, H, H, H, H, 3, OEt, 50°; H, MeO, H, H, MeO, 2,OCH2Ph, 102-3.5°; H, MeO, H, H, MeO, 2, iso-PrO, 104-5°; H, MeO, H, H, MeO, 2, tropyloxy, 125-6°; H, H, H, H, H, 2, OCH2Ph, 57-8°; H, MeO, H, H, MeO, 2, OCH2C6H4NO2-p, 140-1°; H, MeO, H, H, MeO, 2, OCH2C6H4Cl-p, 127-8°; H, MeO, H, H, MeO, 2, OH, 143-4°; H, MeO, H, H, MeO, 2, OMe, 106-8°; H, MeO, H, H, MeO, 2, OCH2CH:CH2, 89.5-90.5°; H, Cl, Cl, Cl, Cl, 2, NeEt2, 107°; H, Cl, Cl, Cl, Cl, 2, NHPh, 248-9°; H, H, NO2, H, H, 2, NEt2, 78-9°; H, H, NO2, H, H, 2, OH, 166-7°; H, H, NH2, H, H, 2, NEt2, 139.5-41.5°; H, NO2, H, H, H, 2, NEt2, 74-5°; H, NH2, H, H, H, 2, NEt2, 96-8°; Ph, H, H, H, H, 2, NEt2, 102°; Ph, H, H, H, H, 2, NMe2, 128-9°; H, H, H, H, H, 3, Cl, 72.5-4.5°; H, H, H, H, H, 3, NMe2, 867°; H, H, H, H, H, 3, NMe2, - [L(+)-form [α]D 15.8°]; H, H, H, H, H, 3, NEt2, 65-6°; H, H, H, H, H, 3, morpholinyl, 110°; H, H, H, H, H, 3, piperidinyl, 68-70°; H, OEt, H, H, OEt, 2, NEt2, 92.5-3.5°; H, OEt, H, H, OEt, 2, iso-Pr2N, 104-5°; H, OCH2Ph, H, H, OCH2Ph, 2, iso-Pr2N, 138°; H, OMe, OMe, H, H, 2, NEt2, 93-4°; H, OMe, OMe, H, H, 2, iso-Pr2N, 102-3.5°; H, OMe, Me, H, OMe, 2, iso-Pr2N, 12930°; H, OMe, H, H, OMe, 2, NMe2, 169-70°; H, OMe, H, H, OMe, 2, NEt2, 174-5°; H, OMe, H, H, OMe, 2, NPr2, 93-4°; H, OMe, H, H, OMe, 2, iso-Pr2N, 128-9°; H, OMe, H, H, OMe, 2, NHCH2CH:CH2, 169-70°; H, OMe, H, H, OMe, 2, iso-BuNH, 170°; H, OMe, H, H, OMe, 2, NH(CH2)3NMe2, 136-7°; H, OMe, H, H, OMe, 2, NHPh, 181-2°; H, OMe, H, H, OMe, 2, piperidinyl, 151-2°; H, OMe, H, H, OMe, 2, N(CH2CH:CH2)2, 110-11°; H, NO2, H, H, OMe, OMe, 2, NEt2, 115.516°; H, OMe, OMe, H, OMe, 2, NEt2, 138-9°; H, OMe, OMe, H, NHAc, 2, iso-Pr2N, 159°; H, Cl, Cl, Cl, Cl, 2, iso-Pr2N, 171-2°; H, H, H, H, H, 2, iso-Pr2N, 81-2.5°; H, OMe, H, H, OMe, 2, NHPr, 189-90 eg/; H, OMe, H, H, OMe, 2, NHCONH2, 234°; H, OMe, OMe, H, H, 2, NHCONH2, 212-13°; H, AcNH, H, H, H, 2, NEt2, 86-7.5°; H, H, H, H, H, 2, NMe2, 86°; H, H, H, H, H, 2, piperidinyl, 59-60°; H, H, H, H, H, 2, morpholinyl, 99.5-100.5°; H, H, H, H, H, 2, N(CH2CH:CH2)2, b0.4 204°, (n25D 1.5570); H, Me, H, H, Me, 2, N(CH2CH:CH2)2, 63-4.5°; H, Me, H, H, Me, 2, NEt2, 98°; H, Me, H, H, Me, 2, piperidinyl, 100.5°; H, NO2, H, H, NO2, 2, OH, 142.5-5.0°; H, Et2N, H, H, NO2, 2, NEt2, 72-4.5°; Ph, H, H, H, H, 2, piperidinyl,

L8 ANSWER 21 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

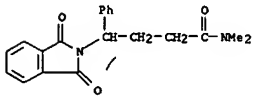
124.5-5.5°; Ph, H, H, H, H, 2, morpholinyl, 1512°; H, H, H, H, H, 3, NMe2, 72-2.5°; H, H, H, H, H, 3, morpholinyl, 88-9°; Me, H, H, H, H, 2, NHBu-tert, 106-8°; Me, H, H, H, H, 2, NHMe, 105-6°; Me, H, H, H, H, 2, OH, 156-8°; H, H, H, H, H, 3, OH, 116-18°; Ph, H, H, H, H, 2, OH, 167°; H, NO2 H, H, H, 2, OH, 134-4.5°; H, NH2, H, H, H, 2, OH, 164-6°; H, NO2, H, H, NO2, 2, OH, 141-2°; H, NO2, H, H, NO2, 2, NH2 213-14°; H, H, H, H, H, 2, NH2, 160-4°; H, NH2, H, H, H, 2, NH2, 195-6°; H, Cl, Cl, Cl, Cl, 2, NH2, 248-9°; H, Cl, H, H, Cl, 2, NH2, 200-2°; H, MeO, H, H, MeO, 2, NH2, 208-10°; H, Ph, H, H, Ph, 2, OH, 186.58°; H, Ph, H, H, Ph, 2, NH2, 205.5-7.0°; H, Me, H, H, Me, 2, OH, 195-6.5°; H, Me, H, H, Me, 2, NH2, 175.5-6.0°; H, H, H, H, H, 3, NH2, 111-12°; H, EtO, H, H, EtO, 2, NH2, 179-80°; Ph, H, H, H, H, 2, NH2, 163-4°; and H, H, H, H, H, 2, OEt, 71-2°. The following compds. were prepd. according to the various procedures given above (m.p. given): 4-homophthalimidobutyric acid, 128.5-30°; ethyl 4-homophthalimidobutyrate (IV), 61.5-2.5°; N,N-dimethyl 4-quinolimidobutyramide, 124-5°; cis-4-(Δ4-tetrahydrophthalimido)butyric acid, 99-102°; N,N-dimethyl cis-4-((Δ4-tetrahydrophthalimido)butyramide, b0.4 192°, n25D 1.5237; N,N-diethyl cis-4-(Δ4-tetrahydrophthalimido)butyramide, b3.03-0.5 170-90°, n25D 1.5214; N,N-dimethyl-4-phthalimidopent-2-eneamide, 79.5-80°; N,N-dimethyl-4-phthalimidohexanamide, -; 4-phthalimidohexanoic acid, 104-5°; 1,3-dioxo-2-(1-carboxybut-3-yl)-4,9-methano-3a,4,9,9a-tetrahydrobenz[f]isoindole, 143-4°; 1,3-dioxo-2-(1-dimethylaminocarbonylbut-3-yl)-4,9-methano-3a,4,9,9a-tetrahydrobenz[f]isoindole, 153-3.5°; 4-methyl-2-pyrrolidinone, b1 89-92°; 4-amino-3-methyl-butyric acid, -; 3-methyl-4-phthalimidobutyric acid, 141-2°; N,N,3-trimethyl-4-phthalimidobutyramide, 82-3°; diethyl 4-methyl-4-nitrovaleramide, b2 144-50°, n19D 1.4681; N,N-diethyl-4-amino-4-methylvaleramide, b0.8 100-2°, n19D 1.4672; N,N-diethyl-4-methyl-4-phthalimidovaleramide, -; dimethyl-4-methyl-4-nitrovaleramide, b0.5 108°, n22D 1.4708; dimethyl-4-amino-4-methylvaleramide -; N,N-dimethyl-4-methyl-4-phthalimidovaleramide, b0.02 160-90°; 2-(1-carboxyprop-1-en-3-yl)sulfobenzimide, 198-9°; 2-(1-dimethylaminocarbonylprop-1-en-3-yl)sulfobenzimide, 164-5°; 2-(1-carboxybut-1-en-3-yl)sulfobenzimide, 162-4°; 2-(1-dimethylaminocarbonylbut-1-en-3-yl)sulfobenzimide, 140-40.5°; 2-(1-N-methyl- N-phenylaminocarbonylbut-1-en-3-yl)sulfobenzimide, 104-5°; 2-(1-ethylaminocarbonylbut-1-en-3-yl)sulfobenzimide, 106-7°; 4-bromohex-2-enoic acid, b0.4 94-8°, n20D 1.5130; 2-(1-carboxypent-1-en-3-yl)sulfobenzimide, 150-2°; 2-(1-dimethylaminocarbonylpent-1-en-3-yl)sulfobenzimide, 142.5-3.0°; 2-(1-carboxypent-3-yl)sulfobenzimide, 85-9°; 2-(1-tert-butylaminocarbonylpent-3-yl)sulfobenzimide, 141-2°; 2-(1-ethyl- aminocarbonylpent-3-yl)sulfobenzimide, 85.5-6°; 2-(1-dimethyl-aminocarbonylpent-3-yl)sulfobenzimide, b0.1 195-205°; 4-bromo-3-methylbut-2-enoic acid, b0.8 98-102°, n20D 1.5230; 2-(1-carboxy-2-methylprop-1-en-3-yl)sulfobenzimide, 182-4°; 2-(1-dimethylaminocarbonyl-2-methylpropyl-1-en-3-yl)sulfobenzimide, 135-6.5°; N,N-dimethyl-4-phthalimidovaleramide, 85°; 3-methyl-3-phthalimidobutyric acid, 118.5-20.5°; N,N-dimethyl-4-methylphthalimidovaleramide, -; 2-(1-dimethylaminocarbonylbut-2-en-3-yl)sulfobenzimide, 119-20°; 2-(1propylaminocarbonylbut-1-en-3-yl)sulfobenzimide, 109-10°; 2-1(-dimethylaminocarbonylbut-1-en-3-yl)sulfobenzimide, 101-2°; 2 - (1 - aminocarbonylprop-3-yl) sulfobenzimide, 151-3°; 4-(3-aminophthalimido)butyronitrile, 91-3.5°; 4-

L8 ANSWER 21 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
(tetrachlorophthalimido)butyronitrile, 194-5°; 4-trifluoroacetamidobutyramide, 108-10°; γ-1,8-naphthalimidobutyronitrile, 115°; 4-(1,8-naphthalimido)butyramide, 233-6°; 4-(3,6-dichlorophthalimido)butyronitrile, 143-4°; 3,6-dimethoxyphthalimidobutyronitrile, 167-9°; 4-phthalylglycylaminobutyramide, 237.5-8.5°; 4-phthalimidovaleryl chloride, 72.5-4.5°; 4-(4,4-diethylhomophthalimido)butyramide, 98-9°; 4-phthalimidobutyryl chloride, 65-8°; 3-(3-cyanopropyl)-3,4-dihydro-4-quinazolone, 85-6.5°; and 3-(3-carbethoxypropyl)-3,4-dihydro-4-quinazolone-HCl, 199-203°.

IT **10264-94-5**, 2-Isoindolinebutyramide, N,N-dimethyl-1,3-dioxo-γ-phenyl- **10264-95-6**, 2-Isoindolinebutyramide, N,N-diethyl-1,3-dioxo-γ-phenyl-
(preparation of)

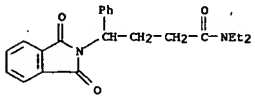
RN 10264-94-5 CAPLUS

CN 2-Isoindolinebutyramide, N,N-dimethyl-1,3-dioxo-γ-phenyl- (7CI, 8CI) (CA INDEX NAME)



RN 10264-95-6 CAPLUS

CN 2-Isoindolinebutyramide, N,N-diethyl-1,3-dioxo-γ-phenyl- (7CI, 8CI) (CA INDEX NAME)



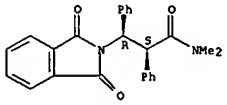
L8 ANSWER 22 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
cyclohexylamino, 90, 227-8°, 87, 230-1°, 75, 153-4°, 60, 162-4°.

IT **6903-74-8**, 2-Isoindolinepropionamide, N,N-dimethyl-1,3-dioxo-α,β-diphenyl-, threo- **6903-75-9**, 2-Isoindolinepropionamide, N,N-dimethyl-1,3-dioxo-α,β-diphenyl-, erythro-
(preparation of)

RN 6903-74-8 CAPLUS

CN 2-Isoindolinepropionamide, N,N-dimethyl-1,3-dioxo-α,β-diphenyl-, threo- (8CI) (CA INDEX NAME)

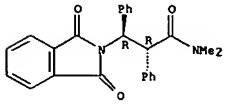
Relative stereochemistry.



RN 6903-75-9 CAPLUS

CN 2-Isoindolinepropionamide, N,N-dimethyl-1,3-dioxo-α,β-diphenyl-, erythro- (8CI) (CA INDEX NAME)

Relative stereochemistry.



L8 ANSWER 22 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1966:103548 CAPLUS

DOCUMENT NUMBER: 64:103548

ORIGINAL REFERENCE NO.: 64:19403e-h,19404a-b

TITLE: Synthesis and configuration of the mono- and dialkyl-substituted amides of the diastereomeric 3-amino-2,3-diphenylpropanoic acids

AUTHOR(S): Stefanovskii, J. N.; Ninova, P.

CORPORATE SOURCE: Bulgarian Acad. Sci. Sofia

SOURCE: Monatshefte fuer Chemie (1966), 97(1), 87-93
CODEN: MOCMB7; ISSN: 0026-9247

DOCUMENT TYPE: Journal

LANGUAGE: German

OTHER SOURCE(S): CASREACT 64:103548

AB PhCH2CONMe2 (I), cyclohexylamide (II), and morpholide (III) of PhCH2CO2H (IV) with (PhCH:N)2CHPh (V) in the presence of AlCl3 yielded mixts. of the amides of the diastereomeric 3-amino-2,3-diphenylpropanoic acids (VI). The configurations of the amides were proved by their synthesis from the corresponding VI and secondary amines. The appropriate amide (0.02 mole) and 0.01 mole V in 10 cc. dry C6H6 treated with cooling with 0.02 mole AlCl3 in portions, heated 2 hrs. at 90°, cooled, diluted with 15 cc. 1:1 HCl-H2O, and blown with steam, and the distillation residue basified gave the corresponding amide of the VI. I gave 40% (+)-threo-PhCH(NH2)CHPhCONMe2 (VII), m. 156-7° (H2O). VII in dry Et2O with HCl-Et2O yielded VII.-HCl, m. 158-63° (decomposition) (EtOH-Et2O). The mother liquor from the VII gave further 0.26 g. mixture of VII and the erythro isomer (VIII) of VII, and then 0.62 g. VIII, m. 119-21° (heptane); VIII.HCl m. 215-16°. The original steam distillate contained 98% BzH and 93% I. II gave similarly 12% cyclohexylamide (IX) of (+)-threo-PhCH(NH2)CHPhCO2H (X), m. 163-4.5°; [IX.HCl m. 230.5-31° (EtOH-Et2O)], and 0.8 g. cyclohexylamide (XI) of the erythro isomer (XII) of X.HCl, m. 227.5-28° (repptd. from EtOH with Et2O). XI.HCl with base yielded 85% XI, m. 153-4°. The original steam distillate gave 95% each BzH and II. III yielded similarly 2.61 g. crude amino bases which dissolved in 20 cc. EtOH and treated 4-5 hrs. with 1 cc. BzH and 5 cc. 10% aqueous NaOH gave 3.09 g. morpholide (XIII) of threo-PhCH(N:CHPh)CHPhCO2H (XIV), m. 194-6° (EtOH), and 0.89 g. morpholide (XV) of the erythro isomer of XIV, m. 144-6° (heptane). XV(0.48g.)and 10cc. 1:2HCl distilled to remove all BzH, basified, and extracted with Et2O, and the extract treated with HCl gave the morpholide of XII.HCl, m. 229-9.5° (repptd. from EtOH with Et2O). XIII (0.8 g.) gave similarly 0.52 g. morpholide of X, m. 153-4°; HCl salt m. 157.5-60° (decomposition). XIII (0.5 g.) stirred 3 hrs. at room temperature with 0.38 g. LiAlH4 in dry Et2O yielded 0.44 g. pale yellow oil which gave 0.48 g. (+)-threo-N-(3-benzylamino-2,3-diphenylpropyl)morpholine-HCl, m. 251-2° (EtOH-Et2O). Chloride (0.39 g.) of erythro- or threo-3-phthalamido-2,3-phenylpropionic acid in 8-10 cc. dry Me2CO treated 15-20 min. with excess amine yielded the corresponding XVI (R, and % yields and m. ps. of erythro and threo isomers given): Me2N, 90, 211-12.5°, 84, 235-6°; morpholino, 81, 176-7°, 96, 197-9°; cyclohexylamino, 78, 215-16°, 87, 228.5-29°. The appropriate XVI (0.01 mole) and a slight excess N2H4.H2O in 6 cc. EtOH heated 1 hr. on a water bath and then 0.5 hr. with 3 cc. 6N HCl yielded the corresponding PhCH(NH2)CHPhCONR2 (NR2, % yields and m. ps. of HCl salts of erythro and threo isomers and % yields and m. ps. of erythro and threo bases given): Me2N, 75, 215-16°, 70, 159-63°, 54, 119-21°, 67, 156-7°; morpholino, 78, 225-6° (semiliquid), 74, 158-61°, --, --, 71, 152-3°;

```
=> lo gy
LO IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> log y
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   109.13     432.45

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                   -16.06     -16.06

STN INTERNATIONAL LOGOFF AT 13:15:18 ON 04 MAR 2005
```